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THE ELECTROMETRIC TITRATION OF THE
PLASMA AS A MEASURE OF ITS
ALKALINE RESERVE

DISSERTATION

SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR
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BY

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STUDIES OF ACIDOSIS.

III. THE ELECTROMETRIC TITRATION OF PLASMA AS A MEASURE OF ITS ALKALINE RESERVE.

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It has been definitely established that the reaction of the blood is, under normal conditions, constant (Lundsgaard, 1912) and may be kept constant even under pathological conditions involving great lowering of the alkaline reserve (Michaelis, p. 105; Benedict, 1906; Peabody, 1914; for more detailed discussion see Paper I of this series). Consequently, the hydrogen ion concentration (C_H) of the blood as drawn from the veins cannot be taken as an indicator of the alkaline reserve.

We may expect, however, that when a given amount of acid is added to the blood, the resultant change in C_H will be greater the less the reserve alkali; or conversely, that less acid will be necessary to produce a given increase in C_H . The latter principle is essentially that used in methods for titration of the blood with indicators, acid being added until the C_H is reached at which the indicator changes color; and titration methods have contributed greatly to our knowledge concerning the alkaline reserve of the blood and its changes in acidosis (Jaksch, Magnus-Levy, Pembrey, and Spriggs). The interpretation of such results, however, is clouded by two deficiencies inherent in the method. First, the indicators (Bjerrum, 1915), such as methyl orange, which can be used to titrate carbonates as alkali change color at such a high C_H that the titration measures, in addition to the bicarbonate, also an acid binding power of the proteins quite out of proportion to the amounts of acid which these substances can bind within the limits of C_H possible in life (the phosphates of whole blood also act as buffers like proteins, but they play a minimal rôle in plasma). Second, the proteins dimin-

ish by their buffer effect and by absorption of indicator the sharpness of the end-points, and thereby decrease the accuracy of the titrations. Attempts to overcome these difficulties by precipitating the proteins with neutral agents such as ammonium sulfate are criticized because the precipitated protein carries down with it a considerable part of the alkali (Hoppe-Seyler). Of the above two difficulties the first is inherent in every mode of titrating blood against strong acids. The second, however, can be avoided by determining the C_H of the end-point electrometrically instead of by indicators, so that even with small amounts of blood or plasma results reproducible with a high degree of accuracy can be obtained. The present paper presents the results of an attempt to develop the electrometric titration into a form practicable for use with normal and pathological plasmas,—and the comparison of the method so developed with the determination of the carbon dioxide combining capacity of the plasma (Van Slyke and Cullen, 1917), and of the carbon dioxide tension of the alveolar air (see Paper VI of this series).

The principles of the gas chain method and its practice have been so thoroughly reviewed in recent literature (Soerensen, 1912; Hildebrand, 1913; Michaelis, 1914; Clark and Lubs, 1916) that only the necessary details are given here.

Apparatus.

All determinations of the H^+ concentration were made by use of the well known gas chain.



The mercury for the calomel cells was purified in the wet way, distilled three times by Hulett's method (1911), and filtered. The calomel was made from this mercury by the method of Loomis and Acree (1911).¹ The N/10 KCl solution was prepared by weight from recrystallized Kahlbaum's KCl and the standardi-

¹ Electrodes prepared from this calomel have not been very satisfactory. In later work with the gas chain the calomel has been prepared electrolytically as described by Ellis (1916). The calomel has been kept under acid and prepared for use by washing by decantation only. Cells prepared from such calomel remain entirely constant for long periods.

zation verified by chloride determinations by the McLean and Van Slyke method.

The hydrogen was taken from tanks of the Standard Oxygen Company and was washed through solutions of HgCl_2 , KMnO_4 , pyrogallol (twice), dilute H_2SO_4 , and water. This proved to be a convenient and satisfactory source of hydrogen.

The electrodes were made from No. 16 and No. 18 platinum wire sealed into glass tubes and platinized with platinum black. Small Clark electrode vessels of about 2 cc. capacity were used, together with the ingenious Clark shaking device (Clark, 1915). This vessel is similar in principle to that of Hasselbalch (1911, 1913), but is superior to it both practically and theoretically. It is designed to give maximum surface of solution and elimination of dead space, and to reduce the contact potential between the solution and saturated KCl solution to a negligible quantity. It is easily manipulated, requires only a small amount of fluid, and gives such thorough contact of solution and electrode that equilibrium is established inside of a few minutes. This apparatus is especially convenient when working with carbon dioxide containing fluids, for it allows easy and economical renewal of the solution without change of hydrogen, the procedure proposed by Hasselbalch. The substitution of a 60° 3-way stop-cock with a 2-way key for the lower stop-cock of the Clark vessel is a decided convenience.

Several calomel electrodes were kept on hand, and compared frequently with one another. An absolute standard was thus maintained, and the readings corrected with it. Weston cells calibrated by the Bureau of Standards gave the standard potential. The readings were taken during the earlier part of the work with a bridge of 1,110 ohms resistance boxes and electrometer as zero point instrument. The external resistance was so adjusted that ohms equalled millivolts. Later a Leeds and Northrup potentiometer with a galvanometer as zero point instrument was installed.

The determinations were run at room temperature, $18-24^\circ$, and temperature corrections applied. The accuracy of the entire determination was tested often by means of Soerensen's standard phosphate and Walpole's standard acetate mixtures of known hydrogen ion concentration.

The N/50 acid used in the titrations was prepared by weight from a standard HCl prepared by Hulett and Bonner's (1909) method and checked by gravimetric silver chloride determinations.

Hasselbalch and Gammeltoft (1915) report that freshly platinized electrodes are essential. Our experience entirely corroborates this observation. The electrodes were always carefully cleaned before each determination in accordance with the following routine. The washed electrodes were placed as cathode in the reducing vessel containing 5 per cent H_2SO_4 for 3 minutes where the bubbling hydrogen removed a considerable quantity of precipitated protein that could not be washed off. Then they were rinsed with water, placed as cathode in the platinic chloride solution for 2 minutes, rinsed, returned to the reducing vessel for 3 minutes, rinsed thoroughly with tap water, and finally with distilled water. The electrodes were often checked against the standard solutions.

Calculation of Results.

All H^+ concentrations are expressed by Soerensen's symbol pH, the negative Briggs logarithm of the hydrogen ion concentration. pH values are more easily visualized and plotted than those of C_H , the actual hydrogen ion concentration. The equation for the calculation of results was:

$$\log \frac{1}{\text{C}_\text{H}} = \text{pH} = \frac{\text{E} - 0.337}{0.0577 [1 + (t^\circ - 18^\circ) 0.0002]}$$

In our work the variations in potential and temperature were such that it was most convenient to construct tables giving pH directly from the observed readings. We used the rounded value of 0.337 for the N/10 calomel electrode adopted by the Potential Commission (Auerbach).

Preparation of Solution.

All our determinations have been made on plasma rather than whole or defibrinated blood; because removal of the corpuscles eliminates the greater part of the oxygen and consequently allows much quicker reduction of the solution by the hydrogen electrode.

The blood was drawn into a tube containing a small amount of powdered potassium oxalate (always less than 0.5 per cent) to prevent clotting, centrifuged at once, and the plasma pipetted off. Experiments proved that the oxalate had no effect on the determination. If it was impossible to run the determination at once, the plasma was placed in a stoppered paraffined tube in the refrigerator.

In comparing the alkaline reserve of different plasmas by titration with acid, two methods are available. First, the amount of acid required to bring the plasma to a definite H^+ concentration may be determined by a series of determinations and consequent plotting of the titration curve. Or, second, the H^+ concentration resulting from the addition of an arbitrarily fixed amount of acid may be found. This is the most economical, both of time and blood, the deciding considerations when series of observations on a number of patients are desired. We therefore used the former only to select suitable conditions to use in this investigation.

However, since the initial reaction of all plasmas is practically constant and the titration curve is almost a straight line, it is entirely possible to construct the curve from one determination and from it determine the amount of acid required to bring the plasma to any desired reaction.

It is evident from the analysis of the equilibrium $\frac{H_2CO_3}{NaHCO_3}$ that all samples must be brought to a definite CO_2 content. The conditions under which the blood is drawn, the time elapsing before determination, etc., are so variable that the plasma cannot be used as it is. Its CO_2 content must either be fixed under definite conditions, or the CO_2 must be removed.

Two procedures have been followed. The first was worked out for and used throughout the investigation of the first series of experiments on diabetic acidosis; the second was developed on the basis of experience with that series.

Technique of Determination.

Procedure A.—It was found that two successive shakings in an evacuated vessel, as described in the next paragraph, reduced the CO_2 content to a fairly constant level. Experiments with

N/50 HCl showed that more than three volumes of this acid per volume of plasma precipitated some of the proteins. The addition of one volume of N/50 acid to one volume of plasma (Fig. 1) brought normal plasma to about the neutral point. Plasma with less than normal alkaline reserve would, under the same conditions, fall on the acid side of the neutral line.

The oxalated blood was centrifuged and the plasma pipetted off. About 3 cc. of the plasma were placed in a 300 cc. separatory funnel, which was evacuated by means of a water aspirator to a pressure of about 20 mm. The funnel was then rotated for 3 minutes to insure maximum surface and permit the escape of carbon dioxide from the solution. Air was then admitted, the funnel was evacuated, and was again rotated for 3 minutes. Exactly 1 cc. of this plasma was then measured into a 3 cc. dropping funnel, and 1 cc. of N/50 HCl added (calibrated 1 cc. pipettes were used for both acid and plasma); the funnel was closed by means of a small rubber stopper and the solution mixed, without shaking. The mixed solution was then allowed to flow through a small piece of rubber tubing into the Clark electrode, displacing part of the hydrogen with which the vessel had been filled. The care taken in mixing and introducing the acidified solution was to prevent loss of CO₂. The vessel was then shaken for 3 or 4 minutes, the electrode adjusted to minimum contact, and the potential read. The vessel was shaken again 3 or 4 minutes, a fresh contact with the saturated KCl solution was made, another reading taken, and the process was continued until equilibrium was reached, which usually was at the second or third reading.

Procedure B.—The method outlined under A is open to the objection that careful attention is required to bring the carbon dioxide to the arbitrary level. This possibility of error can be eliminated by adding enough acid to complete the reaction $\text{NaHCO}_3 + \text{HCl} = \text{NaCl} + \text{H}_2\text{CO}_3$, and then removing all the carbon dioxide by evacuation. The carbon dioxide tension of the plasma is thus eliminated as a factor in the results, and the hydrogen ion concentration is dependent on the equilibrium between the plasma buffers, chiefly the proteins, and the excess of acid not neutralized by bicarbonate. It was found that the addition of two volumes of N/50 HCl to one of plasma was sufficient to effect complete decomposition of the bicarbonate, and the re-

sulting solution after removal of the carbon dioxide showed a C_H of about $10^{-5.6}$ ($pH = 5.6$). At this point the equilibrium in the electrode vessel is obtained much quicker than at the neutral point. This procedure has, over A, the advantages of greater rapidity, the use of smaller amounts of plasma, and the elimination of variations in the carbon dioxide content as a source of error. It has the disadvantage, compared with procedure A, in that the differences in pH corresponding to given differences in "alkaline reserve" are not so great.

In procedure B two volumes of N/50 HCl are added to one of plasma (the amounts being usually 2 and 1 cc. respectively) in a small separatory funnel, 25 to 100 cc., the solution is exhausted with a water aspirator to about 20 mm., and agitated for 1 minute. One exhaustion completely removes the carbon dioxide. The solution is then transferred to the electrode vessel by a pipette, allowed to displace part of the hydrogen, and the reading obtained in the same manner as in A.

EXPERIMENTAL.

The Determination of the Optimum Amounts of N/50 Acid.

Samples of oxalated plasmas were exhausted twice with the water aspirator and the H^+ of the exhausted plasma determined. Then a series of determinations was made varying the ratio of acid and plasma volume as shown in Fig. 1.

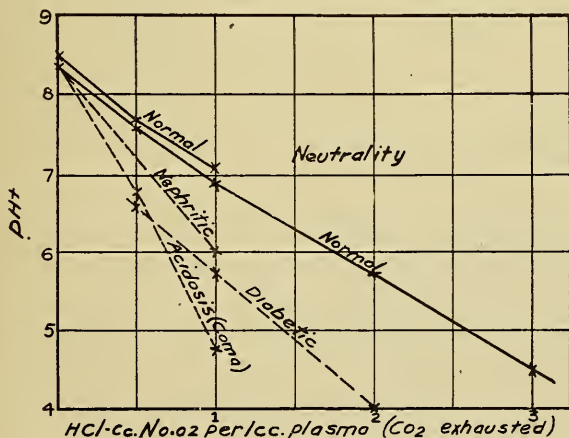


FIG. 1.

It is evident that the addition of one volume of N/50 acid to one volume of plasma brings normal plasma to about the neutral point. The acidosis plasma affords an extreme example of diminished alkaline reserve.

Determination of the Number of Exhaustions Required in Water Aspirator.

Samples of plasma were saturated with alveolar air (5.5 per cent CO₂), portions were placed in separatory funnels, and exhausted on a water aspirator to about 20 mm. for periods of 3 minutes each. During the exhaustion the funnels were rotated constantly to expedite the escape of the CO₂ from the solution. Air was admitted to the funnels between exhaustions. 1 cc. portions were then mixed with 1 cc. portions N/50 HCl in 3 cc. dropping funnels, as described above, and the contents run into the electrode vessels (Table I).

TABLE I.

Number of Exhaustions Needed for Procedure A. pH after Adding One Volume N/50 HCl to Exhausted Plasma.

Human plasma.	Treatment of sample.			
	Saturated with 5.5 per cent CO ₂ .	Exhausted once.*	Exhausted twice.	Exhausted three times.
	<i>pH</i>	<i>pH</i>	<i>pH</i>	<i>pH</i>
1	6.42	6.67	6.69	6.69
2	6.66	6.76	6.78	6.78
3	6.47		6.63	6.63
	6.45		6.62	6.62
4		7.03	7.03	7.03

* Each exhaustion lasted 3 minutes.

It appeared from the above that two exhaustions were sufficient for our purpose, and it was desirable to avoid as far as possible concentrating the plasma by evaporation. Later, however, the perfection of Van Slyke's CO₂ apparatus furnished an accurate and convenient means of checking the above experiments. The amounts of carbon dioxide remaining after successive exhaustions were determined. The plasma was placed in large separatory funnels, the exhaustions were carried out as described under pro-

cedure A, and a 1 cc. sample was removed for analysis after each exhaustion (Table II).

TABLE II.

Number of Exhaustions Needed for Procedure A. Total Residual CO₂ Determined by Van Slyke's Method. Corrected to 0°, 760 Mm.

Human plasma.	Saturated with 6.3 per cent CO ₂ .	CO ₂ remaining after									
		1st 3' exhaustion.	Per cent of CO ₂ at saturation.	2nd 3' exhaustion.	Per cent of CO ₂ at saturation.	3rd 3' exhaustion.	Per cent of CO ₂ at saturation.	4th 3' exhaustion.	Per cent of CO ₂ at saturation.	5th 3' exhaustion.	Per cent of CO ₂ at saturation.
	cc.	cc.		cc.		cc.		cc.		cc.	
G.....	0.79	0.60	76.2	0.54	68	0.49	62	0.48	60	0.45	57
A.....	0.72	0.53	73	0.43	60	0.40	56	0.38	53	0.38	51
An.....	0.75	0.55	73	0.45	60	0.41	54	0.38	51		
O.....	0.775	0.57	74	0.52	67	0.46	59	0.43	55	0.40	51

It is evident from Table II that exhaustion was not complete. This was expected. However, the variations after two exhaustions were so small in their effect on pH, as demonstrated in Table I, that accurately reproducible results are obtainable when two exhaustions, carried out as described, are used as the arbitrary standard.

That the arbitrarily selected double exhaustion approximates to a constant carbon dioxide content is also evident from the curves constructed from these values in Fig. 2.

The carbon dioxide as a source of error has been entirely eliminated in procedure B by the use of larger amounts of acid and exhaustion *after* its addition. The following experiment shows this (Table III).

Two volumes of N/50 acid were added to one volume of plasma in a separatory funnel. The funnel was exhausted to about 20 mm. for 1 minute, with constant rotation. 1 cc. was taken for analysis and the exhaustion repeated.

The amounts of residual gas in column 3 are entirely comparable with the "dissolved air" correction in this method; therefore no measurable amounts of carbon dioxide were present.

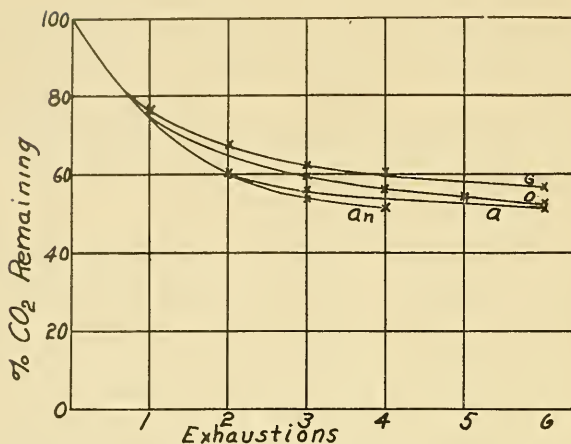


FIG. 2. From Table II.

TABLE III.

Number of Exhaustions in Water Aspirator Needed after Adding Two Volumes of N/50 HCl. Dissolved Gases Determined by Van Slyke's Method. 30° and 762 Mm.

Sample plasma.	Exhausted 3' with shaking. Gas observed.	Dissolved air calculated as present.	CO ₂ present.
	cc.	cc.	cc.
Mixed normal.....	0.04	0.044	0.000
Same saturated with 6.3 per cent CO ₂	0.04	0.044	0.000
A.....	0.045	0.044	0.000
Dog.....	0.04	0.044	0.000
H.....	0.05	0.044	0.000

Comparison of Two Procedures for Removing Carbon Dioxide.

Hydrogen ion concentrations were determined on two plasmas. Each was then divided in two portions, one of which was placed in a separatory funnel and was exhausted 3 minutes as in procedure A. 1 cc. samples were then mixed with various volumes of N/50 acid and the resulting reaction was determined.

To samples of the other portions in separatory funnels varying volumes of N/50 acid were added and the mixtures exhausted

for 1 minute. The results are given in Table IV and plotted in Figs. 3 and 4; it is evident that the two series differ but little.

TABLE IV.
Comparison of Procedures A and B.

Plasma.	$\frac{N}{50}$ acid per cc. plasma.	A (exhausted twice before adding acid).	B (exhausted once after adding acid).
	cc.		
P. pH = 8.63.	0.5	7.73	7.56
		7.74	7.58
	1.0	6.74	6.68
		6.74	
	2.0	5.43	5.34
		5.42	5.33
M. pH = 8.61.	3.0	4.54	4.40
		4.53	4.40
	0.5	7.76	7.83
	1.0	6.88	6.87
	2.0	5.47	5.48

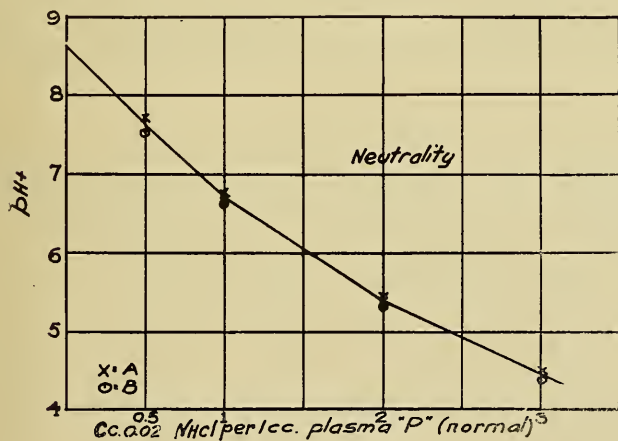


FIG. 3.

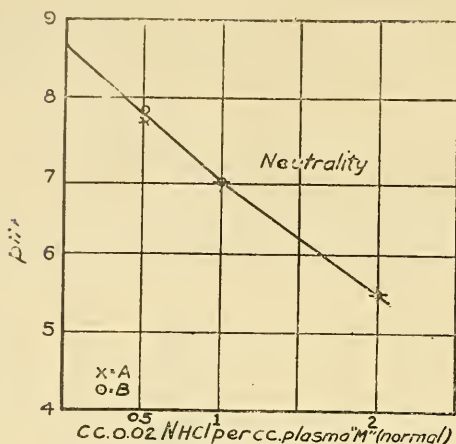


FIG. 4.

Experiment to Determine the Effect of Oxalate on the Titration of Plasma.

Solutions of M/10 phosphates and of normal plasma were made up with varying concentrations of potassium oxalate. H^+ concentration determinations were made as indicated in Table V. It is evident that in plasma oxalate up to 0.5 per cent does not produce an appreciable change and that the change produced by 1 per cent is within the allowable limits of experimental error. About 0.2 to 0.3 per cent is ordinarily sufficient to prevent clotting.

TABLE V.
Effect of Oxalate.

On pH of M/10 phosphate solution concentration.		On pH of M/10 phosphate solution + 1 vol. N/50 HCl concentration.		On pH of normal plasma treated by procedure B (2 vol. N/50 acid added) concentration.	
K oxalate.	pH.	K oxalate.	pH.	K oxalate.	pH.
<i>per cent</i>		<i>per cent</i>		<i>per cent</i>	
0	7.50	0	6.74	0	5.38
0.2	7.47	0.25	6.74	0.5	5.38
0.6	7.47	0.5	6.74	1.0	5.39
1.0	7.44	1.0	6.72	2.0	5.45
1.6	7.45			4.0	5.53
2.0	7.94				

Effect of Renewing Solutions in Electrodes.

Hasselbalch pointed out the possibility of renewing successively the solutions in the electrode without renewing the H_2 as a means of bringing the CO_2 content of the electrode gas to equilibrium with that of the solution. The following experiment (Table VI) shows that this precaution is unnecessary with the small amount of residual CO_2 present under procedure A.

TABLE VI.

Effect of Renewing Solution without Change of H_2 Atmosphere. New Solutions Were Run into the Electrode Vessel Displacing the Used Solution without Changing the H_2 Bubble.

Plasma.	E.	S.	U.	H.	M.	M. 2.	V.
pH of 1st determination...	8.13	7.11	6.48	7.03	6.55	6.89	6.99
pH of renewed solution...	8.14	7.11	6.48	7.03	6.58	6.91	6.99

Accuracy of the Method.

Clark has pointed out the possibility of accuracy attainable with his electrode. With plasma we have considered 1 millivolt = 0.02 pH our permissible error. This amount is very small in comparison with the gross differences we have obtained in the clinical studies.

Table VII gives samples of the results obtained in duplicate determinations.

Titration of Plasma Containing Lactic and β -Oxybutyric Acids.

Since a diminished alkaline reserve is the result of the introduction of abnormal acid products of metabolism, it seemed desirable to investigate the effects of adding such acids to a normal plasma *in vitro*. The results of such experiments are shown in Tables VIII and IX, and Figs. 5 and 6. These experiments were performed as follows:

Experiment I. Curves A and B.—A weighed amount of acid was added to a portion of plasma to make the plasma 0.2 per cent acid solution. This solution was then mixed with untreated plasma in varying proportions and the resulting mixtures were

TABLE VII.

Duplicate Determinations Made with Different Electrodes in Different Vessels.

Procedure A.					Procedure B				
Plasma (human).	Date.	Temperature.	Reading.	pH.	Plasma.	Date.	Temperature.	Reading.	pH.
		°C.	milli-volts				°C.	milli-volts	
A.	May 15	23	723	6.57	Dog VIII.		25	630	4.96
		23	722	6.55			23	627.7	4.96
W.	" 25	24	742	6.87	"	June 14	25	627	4.91
Normal.		23.5	740	6.85			23	626.6	4.93
V.	" 26	23	744	6.93	V.* (human).	" 13	25	650.4	5.30
Normal.		23	744	6.93			26	652.5	5.33
							26	651.6	5.31
M.	" 23	24	749	6.99			26	651.6	5.31
Normal.			749.5	7.00			26.5	652.3	5.32
								652.2	5.32
H.	March 21	20	723	6.64					
		21	723	6.62	Dog 2 a.	" 10	25	620	4.98
							26	622.6	4.91
					" 2 b.	" 10	25	631.5	4.98
							26	632	4.97
					" 3.	" 11	22	630	5.00
								630.1	5.00

* These six determinations were run with six distinct pipettes, funnels, and electrodes, and in two electrode vessels.

titrated by both A and B methods. The acids were analyzed by adding excess N/7 NaOH, warming on a steam bath for a couple of hours, and titrating back with N/7 HCl using phenolphthalein.

	per cent
β -Hydroxybutyric acid analyzed.....	100
Lactic acid analyzed.....	95.2

Experiment II. Curve C.—The acids used in the preceding experiment had not been treated to remove any anhydride that might have been present; the experiment was therefore repeated.

TABLE VIII. .

Effect of Organic Acids on the Titration Curve.

Normality of organic acid on basis of plasma volume only.	A	B
	1 vol. plasma + 1 vol. N/50 acid. Curve A.	1 vol. plasma + 2 vol. N/50 acid. Curve B.
<i>β-Hydroxybutyric acid (Fig. 5).</i>		
	<i>pH</i>	<i>pH</i>
0	6.73	5.34
	6.72	5.35
0.0094	6.55	5.16
	6.55	5.16
0.024	5.84	4.85
	5.84	4.85
0.047	5.08	4.58
	5.07	4.57
0.094	4.59	4.29
	4.58	4.28
0.189	4.15	4.00
		4.00
<i>Lactic acid (Fig. 6).</i>		
0.011	6.26	4.94
	6.24	4.94
0.028	5.355	4.565
	5.345	4.575
0.056	4.58	4.18
		4.18
0.11	4.03	3.83
	4.02	3.83
0.22	3.64	3.48
	3.65	3.48

0.225 gm. of lactic acid was placed in a flask with 30 cc. of N/10 sodium hydroxide, placed on the steam bath for 2 hours, 50 cc. of N/10 HCl were added, and the solution was diluted to 100 cc. The solution was then N 0.025 to lactic acid and N 0.02 to hydrochloric acid.

2 gm. of CaZn β -oxybutyric acid salt were treated with three-fourths of its equivalent sulfuric acid and the liberated acid was extracted with ether in a wet extractor. The ether was evaporated off over water and the solution diluted to 100 cc. The amount of acid was titrated with sodium hydroxide as in lactic

acid. 0.130 gm. of this acid was then treated with 15 cc. of $N/10$ sodium hydroxide heated on the steam bath for 2 hours, 25 cc. of $N/10$ HCl were added, and the solution was diluted to 50 cc. This solution was then N 0.025 to β -oxybutyric acid and N 0.02 to hydrochloric acid.

TABLE IX.
Effect of Organic Acid on the Titration Curve.

Solution A. 1 vol. plasma + 2 vol. $N/50$ HCl.	Solution B.*	Normality of organic acid on basis of plasma volume only.	Lactic acid. Curve C, Fig. 6.	β -Hydroxybutyric acid, Curve C, Fig. 5.
			<i>pH</i>	<i>pH</i>
—	0	0	4.55	4.55
4.0	0.5	0.0055	4.41	4.45
4.0	1.0	0.01	4.32	4.39
4.0	2.0	0.0166	4.20	4.31
3.0	3.0	0.025	4.09	4.24
1.0	3.0	0.037	3.96	4.15
0	—	0.05	3.85	4.07

* Solution: β -oxybutyric acid or lactic acid, N 0.025; hydrochloric acid, N 0.02.

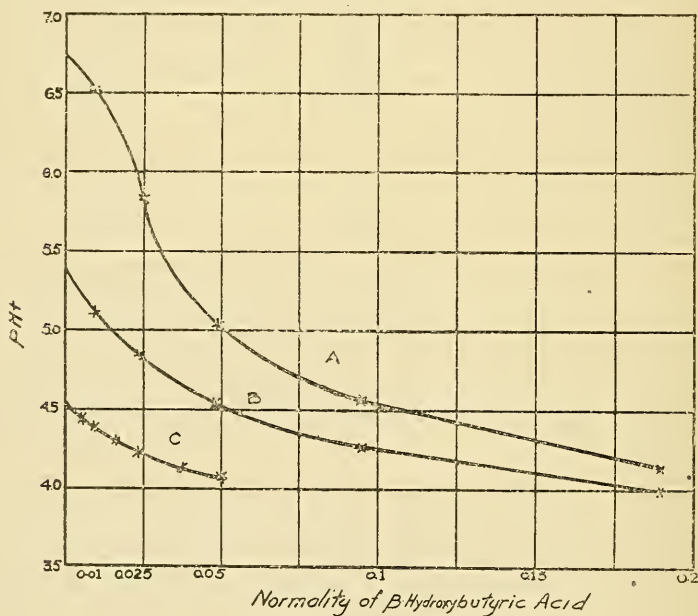


FIG. 5.

The normality figures in A and B do not represent actual amounts of free acid due to the presence of undissociated anhydride, but they do indicate the change in the titration curve caused by the accumulation of such acid. Curve C indicates the nature of the decreased reserve in a dog plasma with very low reserve. The normality figures here represent actual values.

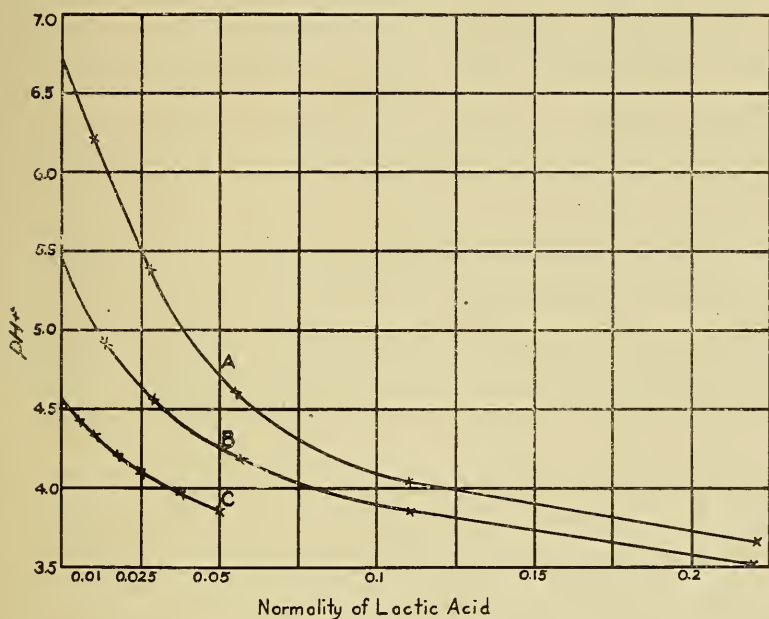


FIG. 6.

Range of Normal Values.

Table X shows the variations in normal plasma in different individuals at different times. The values in a healthy man may change on titration with one volume of $N/50$ acid from a pH of 6.75 to 7.00 during the course of the day. The corresponding figures for titration with two volumes of $N/50$ acid are from a pH of 5.60 to 5.90. Dogs have a lower reserve averaging around a pH of 5.00.

The normal base line for titration with one volume of $N/50$ acid in the accompanying charts is taken at 7.00; with two volumes at 5.6. The normal limits for the "carbon dioxide combin-

ing capacity" is from 55 to 70. The normal alveolar carbon dioxide tension in mm. is about 38. From a number of comparisons the ratio between plasma carbon dioxide volume per cent and alveolar carbon dioxide tension in mm. has been established as 1.45 (see Paper VI).

TABLE X.

Table of Normal Variations.

Procedure A. 1 vol. plasma + 1 vol. N/50 acid.			Procedure B. 1 vol. plasma + 2 vol. N/50 acid.		
Plasma.	Time.*	pH.	Plasma.	Time.	pH.
M.	a. m.	6.80	Dog 1.	a. m.	4.81
	p. m.	6.80		p. m.	5.02
V.	May 15, a. m.	7.04	" 2.	a. m.	5.18
	p. m.	6.89		p. m.	5.24
	" 17, a. m.	6.96	" 3.	a. m.	4.91
	p. m.	6.94		p. m.	5.23
D.	a. m.	7.10	M.	May 18	5.50
	p. m.	7.60		" 22	5.63
P.	a. m.	6.73	F.		5.69
	p. m.	6.84	P.		5.50
S.	a. m.	6.65			
	2 p. m.	6.74			
	4 "	6.71			
	6 "	6.82			
C.	May 19, a. m.	6.58			
	p. m.	6.83			
	"	6.83			
	" 22, p. m.	6.85			

* Indicates before and after meals.

Application of the Method.

The charts of diabetic patients followed for a long period by the electrometric titration of plasma, simultaneously with the determination of CO₂ combining capacity of blood and plasma, alveolar air, and acid excretion, are given in Paper VI of this series.

The values of simultaneous determination of the "carbon dioxide combining capacity" and alveolar carbon dioxide are also shown, since it was one purpose of this series of observations to select the most suitable method for determining the actual amount of "alkaline reserve" in the body.

The samples of blood were obtained from the arm, were drawn through a McRae needle into tubes containing a small amount of potassium oxalate, and centrifuged at once. The determinations were, with a few exceptions, done at once, but samples may be kept for a considerable time in paraffined tubes.

The observations were divided into two periods; the first covering the spring of 1915, the second that of 1916. The electrometric titrations on the first series were done by procedure A — 1 volume of plasma + 1 volume of $N/50$ HCl; on the second series by procedure B — 1 volume of plasma + 2 volumes of $N/50$ HCl. This eliminated the theoretical objection of possible error due to the presence of carbon dioxide, but proved to have the disadvantage of lessening the sensitivity of the titration, in that for given decrease in carbon dioxide combining power the corresponding change in pH was less than with one volume of acid.

CONCLUSIONS.

The conclusions are evident from the charts. The two methods of determining the "alkaline reserve" are entirely comparable and furnish a reliable index of the reserve actually existing in the body. The titration of the plasma includes the influence of all the "buffers," not only the sodium bicarbonate, but also the proteins and the minute amounts of phosphates. The fact that the electrometric titration of the plasma gives results parallel with the carbon dioxide combining capacity indicates that the latter is proportional to the total "buffer" content of the plasma.

SUMMARY.

1. The gas chain method of determining hydrogen ion concentration has been utilized in the titration of plasma and the conditions for successful operation have been determined.

2. Values for normal and pathological plasmas have been determined.

3. The method has been compared with that of the carbon dioxide combining capacity in a long series of diabetic patients, and the close agreement of the two methods has been established.

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APPENDIX.

(pages 413-456.)

Assembly of "charts of diabetic patients" referred to on page 386. (Quoted from a paper by Stillman, Van Slyke, Cullen, and Fitz; *Journal of Biological Chemistry*, 1917, xxx, 413.)

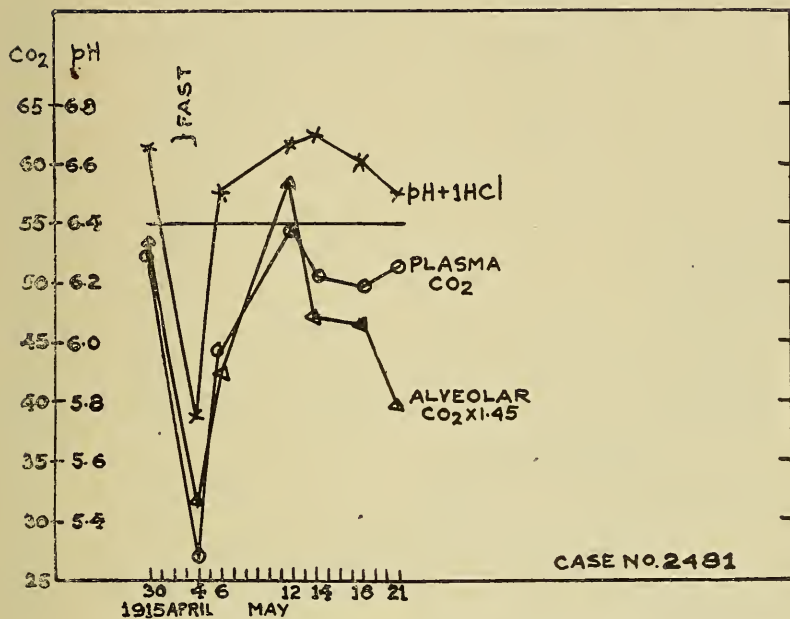
CASES

414 Blood, Urine, and Alveolar Air in Diabetes

1. Case 2481.

Date.	Total calories.	Protein.	Fat.	Carbohydrate.	Alveolar CO ₂ .		CO ₂ bound by 100 cc. plas- ma at 20°.	Ratio plasma CO ₂ mm. alv. CO ₂	Plasma vol. N/50 HCl.
1915		gm.	gm.	gm.	mm.	mm. × 1.45	cc.		pH
Apr. 30	80	7.5	5.0		37.0	53.6	52.2	1.41	6.66
May 1	160	15.0	10.0						
2	Fast day.								
3*	" "								
4	Green veg. only containing			16	21.5	31.2	27.0	1.26	5.75
5	"	"	"	40.5					
6	"	"	"	60.0	29.2	42.3	44.1	1.51	6.51
7†	"	"	"	11.5					
8	375	29.0	25.0	5.0					
9	630	50.0	43.0	"					
10	"	"	"	"					
11	"	"	"	"					
12	"	"	"	"	40.2	58.2	54.5	1.35	6.67
13	"	"	"	"					
14	655	51.5	43.5	10.0	32.4	47.0	50.2	1.55	6.70
15	170†	13.5	12.5						
16	Fast day.								
17	Green veg. only containing			10.0					
18	"	"	"	20.0	32.0	46.4	51.9	1.62	6.61
19†	"	"	"	12.5					
20	Fast day.								
21	355	24.5	23.5	10.0	27.3	39.6	51.2	1.88	6.50

*Drowsiness. †Partial fast.



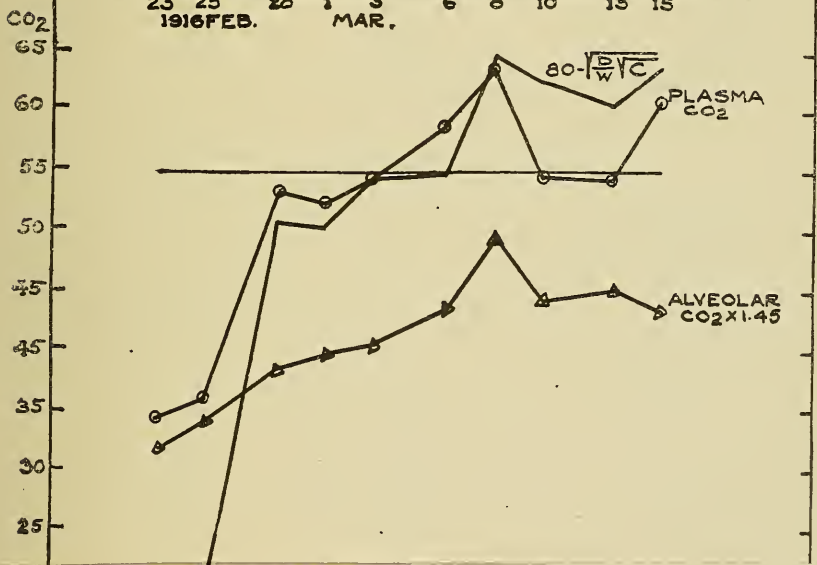
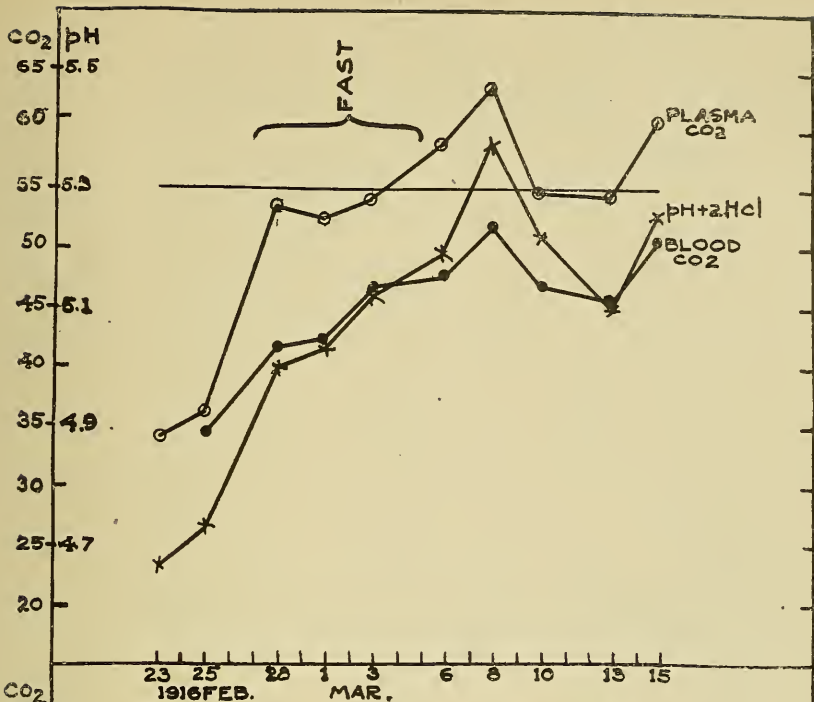
1. Case 2481, female, age 12. Diabetic less than 3 months, mild, fair ability to burn carbohydrate (shown subsequently by a carbohydrate tolerance test).

The curves show a dangerous acidosis when the patient was placed on a fast. This was accompanied by clinical symptoms. The acidosis was ameliorated when a carbohydrate diet was instituted. The drop in alveolar CO₂ on the last day was evidently due merely to change in respiratory control.

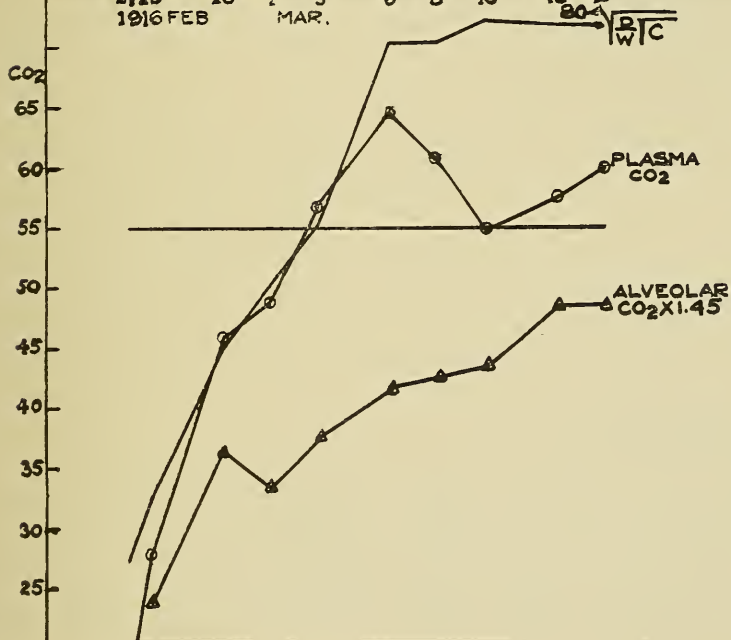
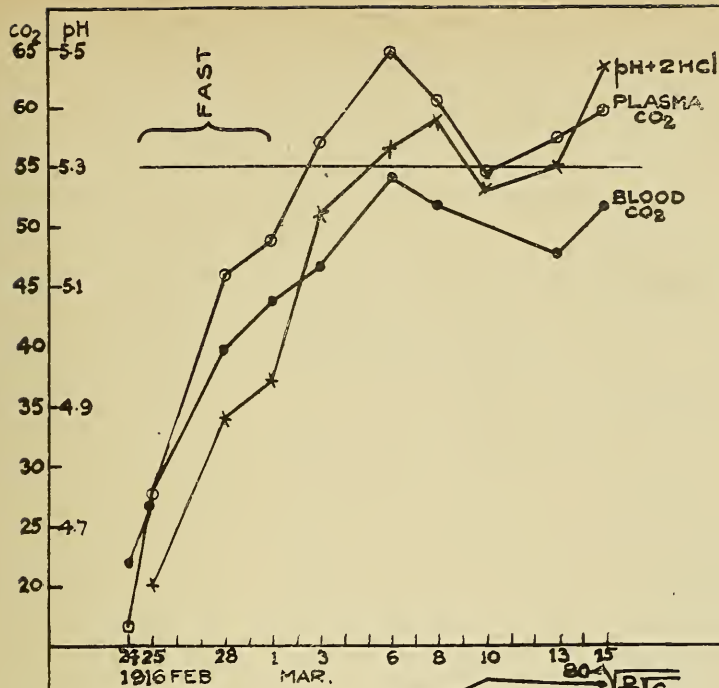
(From April 30-May 21, 1915.)

Group IV.

Date.	Diet.				Body weight.	Blood.						Urine.							
	Total calories.	Protein.	Fat.	Carbohydrate.		Alveolar CO ₂ .	CO ₂ bound by 100 cc. plasma at 20°.	Ratio plasma CO ₂ mm. alv. CO ₂	CO ₂ bound by 100 cc. whole blood at 37°.	Plasma + Vol. HCl. N/50	Vol. per 24 hrs.	Urea per liter.	NH ₃ per liter.	Acid per liter.	$\sqrt{\frac{W}{D}}$	$80 - \sqrt{\frac{W}{D}}$			
1916					gm.	gm.	gm.	gm.	kg.	mm. × 1.45	cc.	cc.	Hd	cc.	cc. N/10	cc. N/10	cc. N/10		
Feb.																			
23*	2,000	75	138	100	37	22.2	31.9	1.54	34.3	4.67	2,600	1,650	1,175	224	60.6	19.4			
24*	"	"	"	"	37.4						2,640	1,440	1,183	204	60.7	19.3			
25*	"	"	127	125	37.6	23.5	34.1	1.53	36.0	4.73	2,560	1,318	1,205	174	59.5	20.5			
26	"	"	"	"															
27	Fast day.																		
28	"	"	"	"	37.7	26.4	38.3	2.02	53.4	5.0	2,625	390	456	54	29.1	50.9			
29	"	"	"	"															
Mar.																			
1	"	"	"	"	37.2	27.3	39.6	1.91	52.1	5.03	1,950	650	568	74	29.7	50.3			
2	"	"	"	"															
3	"	"	"	"	35.6	28.0	40.6	1.93	54.0	5.12	2,305	530	420	62	26.1	53.9			
4	"	"	"	"															
5	Green veg. only containing			10															
6	"	"	"	20	35.6	30.0	43.5	1.97	58.9	5.19	2,140	754	423	64	25.2	54.8			
7	"	"	"	"															
8	"	"	"	8.6	36.9	34.1	49.5	1.86	63.4	5.38	3,045	424	182	22	15.7	64.3			
9	80	7.5	5.0																
10	160	15	10.5		36.3	30.5	44.2	1.80	54.9	5.22	2,600	598	232	28	17.3	62.7			
11	320	30	21.0																
12	Fast day.																		
13	Green veg. only containing			10.0	36.3	31.2	45.2	1.74	54.4	5.10	2,470	556	270	32	19.7	60.3			
14	"	"	"	20.0															
15	"	"	"	30.0	35.8	29.8	43.2	2.04	60.9	5.26	3,010	416	164	60	16.5	63.5			

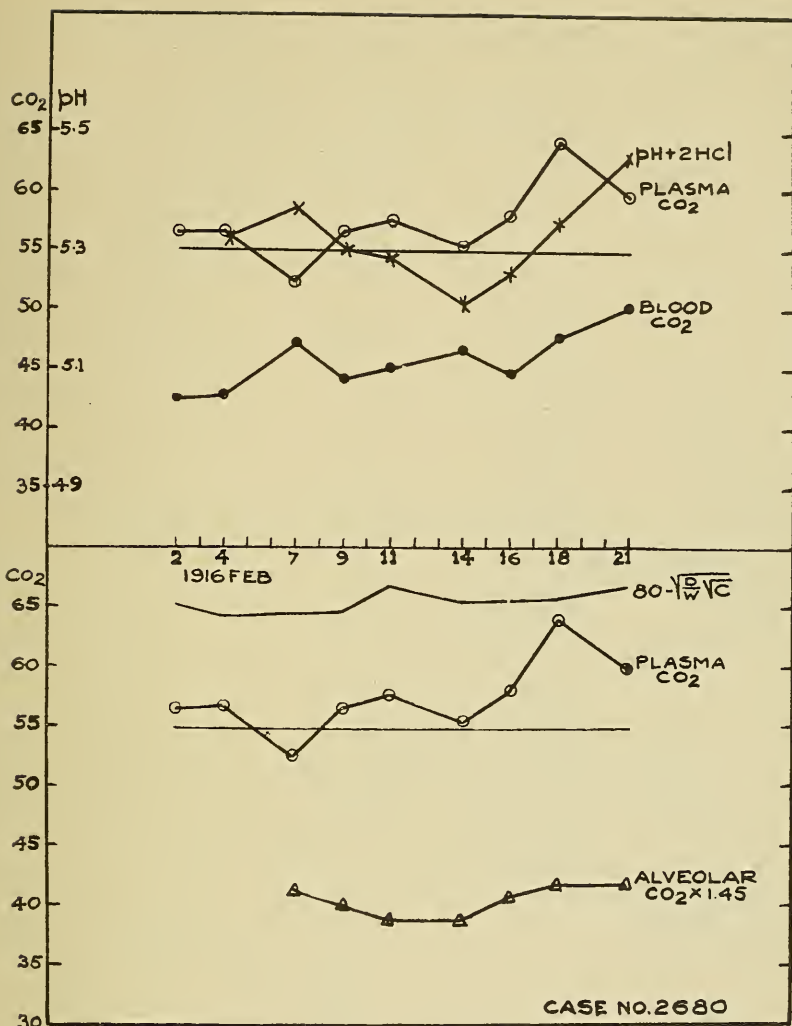


Date.	Diet.				Body weight.	Blood.						Urine.				
	Total calories.	Protein.	Fat.	Carbohydrate.		Alveolar CO ₂ .	CO ₂ bound by 100 cc. plasma at 20°.	Ratio plasma CO ₂ mm. alv. CO ₂	CO ₂ bound by 100 cc. whole blood at 37°.	Plasma + 2 vol. HCl. N/50	Vol. per 24 hrs.	Urea per liter.	NH ₃ per liter.	Acid per liter.	$\sqrt{\frac{D}{W} \vee C}$	$80 - \sqrt{\frac{D}{W} \vee C}$
1916	gm.	gm.	gm.	gm.	kg.	mm. X 1.45	cc.	mm. alv. CO ₂	cc.	pH	cc.	cc. N/10	cc. N/10	cc. N/10		
Feb. 24*	Fast day.				25		16.6		21.9		1,800	2,110	747	230	52.8	27.2
25	"	"	"	"	25.6	16.3	27.7	1.70	27.5	4.61	2,905	1,165	580	144	47.1	32.9
26	"	"	"	"												
27	"	"	"	"												
28	"	"	"	"	25.2	25.0	45.9	1.83	39.6	4.88	3,440	692	370	44	35.1	44.9
29	"	"	"	"												
Mar.	Green veg. only containing				25.3	23.0	48.7	2.12	43.8	4.94	3,675	682	304	28	29.8	50.2
1	"	"	"	"	20											
2	"	"	"	"	30											
3	"	"	"	"	26.4	25.9	56.9	2.20	46.5	5.22	3,300	532	260	20	24.8	55.2
4	"	"	"	"												
5	"	"	"	"	50											
6	"	"	"	"	60	28.6	64.6	2.26	54.0	5.33	3,025	656	99	-12	9.7	70.3
7	"	"	"	"	70											
8	"	"	"	"	80	29.2	60.7	2.08	51.6	5.38	3,165	750	70	10	9.7	70.3
9	"	"	"	"	90											
10	"	"	"	"	100	29.8	54.5	1.83		5.26	3,260	772	57	4	7.9	72.1
11	"	"	"	"	110											
12	"	"	"	"	120											
13	"	"	"	"	130	33.3	57.3	1.72	47.5	5.30	2,655	960	55	18	8.1	71.9
14	"	"	"	"	140											
15	"	"	"	"	25.8	33.3	59.9	1.80	51.9	5.48						



Date.	Diet.					Body weight.	Blood.					Urine.						
	Total calories.	Protein.	Fat.	Carbohydrate.	Alcohol.		Alveolar CO ₂ .		CO ₂ bound by 100 cc. plasma at 20°.	Ratio plasma CO ₂ mm. alv. CO ₂	CO ₂ bound by 100 cc. whole blood at 37°.	Plasma + 2 vol. HCl. N/50	Vol. per 24 hrs.	Urea per liter.	NH ₃ per liter.	Acid per liter.	$\sqrt{\frac{D}{W} \sqrt{C}}$	$80 - \sqrt{\frac{D}{W} \sqrt{C}}$
							mm.	mm. $\times 1.45$										
1916						kg.			cc.	cc.	pH	cc.	cc.	cc. N/10	cc. N/10	cc. N/10		
Feb.																		
2	765	22.5	16	0	75	38.0			56.3	42.3		2,855	792	138	63	14.9	65.1	
3	805	32.5	"	"	"													
4	"	"	"	"	"	37.4			56.4	42.6	5.32	2,540	1,465	190	54	15.9	64.1	
5	"	"	"	"	"													
6	525	Fast day.																
7	650	32.5	16	0	53	37.2	28.4	41.2	57.3	2.02	47.0	5.37	2,015	1,690	195	84	15.6	64.4
8	"	"	"	"	"													
9	625	25.0	"	"	"	38.0	27.6	40.0	56.6	2.05	44.0	5.30	2,065	1,190	202	74	15.5	64.5
10	450*	7.5	5.5	"	"													
11	370	Fast day.				37.7	26.8	38.9	67.8	2.16	45.0	5.29	2,425	1,285	147	46	13.1	66.9
12	450*	7.5	5.5	0	53													
13	505	"	9.5	"	"													
14	530	15.0	10.5	"	"	38.0	26.8	38.9	55.2	2.06	46.6	5.21	2,710	925	158	52	14.7	65.3
15	610	22.5	16.0	"	"													
16	440	15.0	10.5	"	40	37.9	28.1	40.8	58.0	2.06	44.5	5.26	2,380	1,250	214	58	16.7	63.3
17	"	"	"	"	"													
18	320	4.0	2.5	"	"	37.6	28.8	41.8	64.1	2.22	47.9	5.35	2,730	925	167	36	14.4	65.6
19	360*	7.5	5.5	"	"													
20	"	"	"	"	"													
21	400	11.0	8.0	"	"	37.2	28.8	41.8	59.9	2.08	50.1	5.46	2,865	902	147	34	13.3	66.4

* Partial fast.



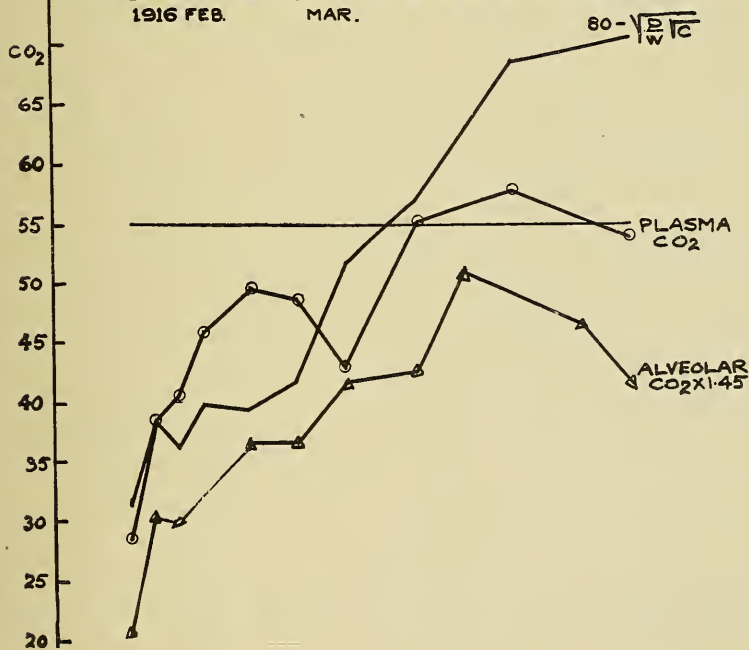
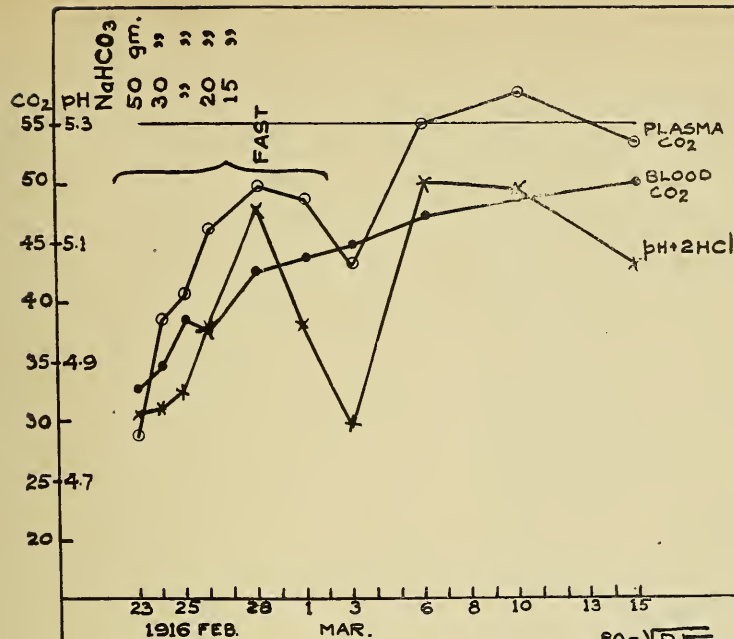
4. Case 2680, female, age 29. Diabetic 10 months, of the extremest type, as shown by the inability to tolerate the 1,000 calories allowed although nearly half of the caloric intake was composed of alcohol. A moderate acidosis was manifested on admission (October 16, 1915).

The curves (taken during the 4th month of hospital observation) show a tendency to acidosis by continually approaching the lower border of normal. Possibly this is the result of the necessarily low diet. The alveolar CO₂ is much too low to show the true blood bicarbonate.

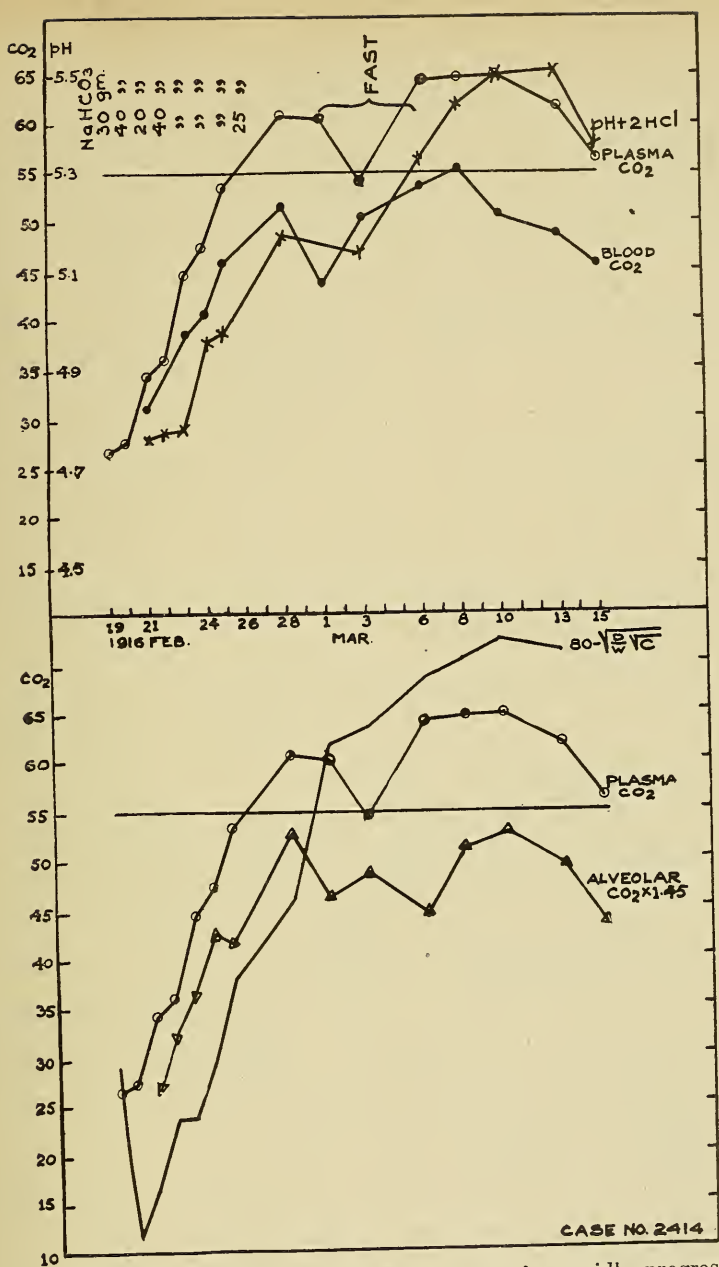
(From February 2-21, 1916.)

Group III.

Date.	Diet.				Body weight.				Blood.					Urine.									
	Total calories.	Protein.	Fat.		Carbohydrate.	gm.	NaHCO ₃ .	kg.	mm.	Alveolar CO ₂ .	mm.X1.46	cc.	Ratio plasma CO ₂ mm. alv. CO ₂	CO ₂ bound by 100 cc. plasma at 20°.	CO ₂ bound by 100 cc. whole blood at 37°.	Plasma + 2 vol. HCl. n/50	Vol. per 24 hrs.	Urea per liter.	NH ₃ per liter.	Acid per liter.	$\sqrt{\frac{D}{W} \sqrt{C}}$	$80 - \sqrt{\frac{D}{W} \sqrt{C}}$	
1916																							
Feb.																							
22*	Fast day.					45		27.8	14.0	20.3	28.6	2.04	32.7	4.81	6,530	915	310	128	48.7	31.3			
23**	" "					50		26.0	20.8	30.2	38.3	1.84	33.5	4.82	4,915	732	317	128	42.6	38.4			
24†	" "					30		25.4	20.6	29.9	40.4	1.96	38.3	4.85	4,760	718	362	112	43.9	36.1			
25†	" "					30		25.0			46.0		37.8	4.97	3,115	888	481	92	40.1	39.9			
26	" "					20																	
27	" "					15																	
28	" "							25.4	25.3	36.7	49.6	1.96	42.8	5.16	3,335	575	483	60	40.7	39.3			
29	" "																						
Mar.																							
1	" "							25.0	25.2	36.5	48.7	1.93	43.8	4.96	3,085	482	336	36	38.5	41.5			
2	Green veg. only containing				10			25.6	20.88	41.8	43.0	1.49	44.7	4.79	1,635	862	526	38	28.3	51.7			
3	" "				20																		
4	" "				"																		
5	" "				"																		
6	" "				25																		
7	" "				"			30.0	29.2	42.3	55.0	1.89	47.0	5.20	2,330	464	342	20	23.1	56.9			
8	" "				"																		
9	" "				30			31.8	28.5						2,965	436	185	14	16.5	63.5			
10†	" "				35			31.6	35.5	50.8	57.6	1.62	48.5	5.19	2,820	502	113	60	11.7	68.3			
10†	" "				8.8																		
11	Fast day.																						
12	Green veg. only containing				5																		
13	" "				10			29.8	31.9	46.3					3,145	474	116	18	9.8	70.2			
14	" "				20																		
15	" "				"			29.4	28.4	41.2	53.6	1.88	50.0	5.06	3,520	332	69						



Date.	Total calories	Protein.	Fat.	Carbohydrat	NaHCO ₃	Body weight	Alveolar CO ₂		CO ₂ bound b 100 cc. plas ma at 20°.	Ratio plasma CO ₂ mm. alv. CO ₂	CO ₂ bound b 100 cc. whol blood at 37°	Plasma + vol. HCl. N/2	Vol. per 24 hr	Urea per litre	NH ₃ per liter	Acid per liter	$\sqrt{\frac{D}{W} \cdot C}$	$80 - \sqrt{\frac{D}{W}}$
		gm.	gm.	gm.	gm.	kg.	mm.	mm. X 1.45	cc.		cc.	pH	cc.	cc. N/10	cc. N/10	cc. N/10		
1916																		
Feb.																		
19*	845	162.5	19	0	30	44.6			26.4				1,130	3,470	1,110	544	50.8	29.2
20	600	94.	23	"	40	44.9			24.2				3,775	3,480	1,102	352	68.56	11.4
21	"	"	"	"	20	44.8	18.0	26.1	34.3	1.90	31.0	4.86	3,980	4,010	1,025	252	63.6	16.4
22	"	"	"	"	40	44.6	22.3	32.2	36.0	1.61		4.87	3,620	3,885	1,065	264	61.4	18.6
23	400	63.	15	"	"	44.6	25.0	36.3	44.5	1.78	38.3	4.88	4,005	3,910	955	248	61.4	18.6
24	"	"	"	"	"	45.0	20.4	42.6	47.2	1.61	40.4	4.96	3,395	3,685	833	208	55.0	29.5
25	"	"	"	"	"	46.0	28.4	41.2	53.3	1.88	45.6	4.98	3,375	3,040	624	200	42.0	38.0
26	200	31.5	7.5	"	25				65.5									
27	"	"	"	"	"				60.9	1.67	51.3	5.18	5,610	2,080	339	122	34.1	45.9
28	"	"	"	"	"	48.9	36.4	52.8										
Mar.																		
1	Fast day.								60.2	1.90	43.3		5,080	1,240	175	60	19.3	60.7
2	"																	
3	"								54.0	1.60	50.3	5.14	3,450	1,235	179	60	16.9	63.1
4	"																	
5	"																	
6	Green veg. only containing			10		47.0	37.0	44.5	64.1	1.73	53.1	5.33	3,290	1,060	117	32	11.4	68.6
7	"	"	"	10														
8	"	"	"	15		47.2	35.5	51.5	64.4	1.81	55.1	5.44	3,500	1,140	100	18	9.7	70.3
9	"	"	"	20														
10	"	"	"	25		46.2	35.5	51.5	64.8	1.82	50.5	5.50	3,175	895	830	8	7.6	72.4
11	"	"	"	30														
12	"	"	"	3.3														
13	160	15	10	0		44	43.1	49.5	61.7	1.81	48.9	5.51	3,315	1,095	78	24	8.8	71.2
14	240	22.5	16	0														
15	Green veg. only containing			10.0		44.4	29.8	43.2	56.2	1.89	45.2	5.34	3,275	1,042	97	24	10.0	70.0



CASE NO. 2414

6. Case 2414, male, age 17. Diabetic 1 year of a rapidly progressive type. Extreme acidosis on his first admission (March 19, 1915), responded

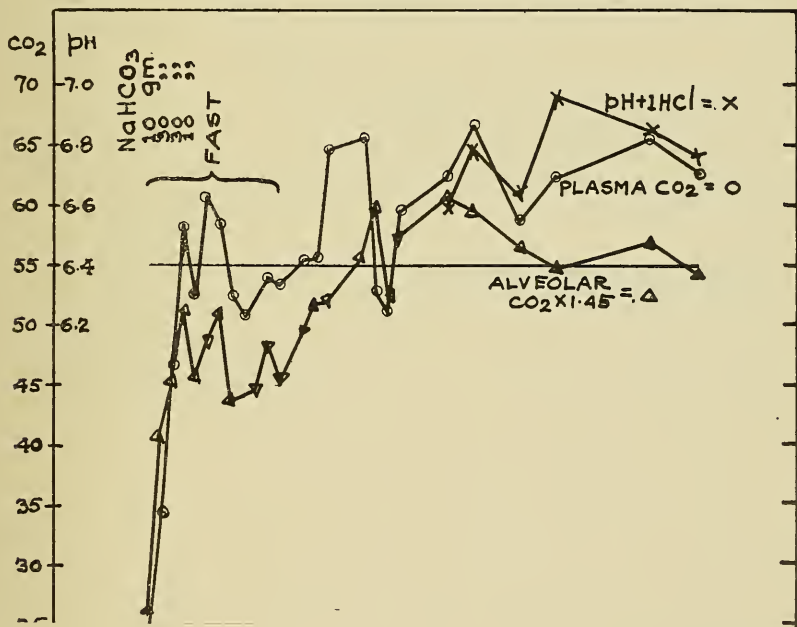
Date.	Total calories.	Protein.	Fat.	Carbohydrate.	NaHCO ₃ .	Alcohol.	Alveolar CO ₂ .		CO ₂ bound by 100 cc. plas- ma at 39°.	Ratio plasma CO ₂ mm. alv. CO ₂ .	Plasma + 1 vol. N/50 HCl.
1915	gm.	gm.	gm.	gm.	gm.	cc.	mm.	mm. × 1.45	cc.		pH
Mar.											
19*	245	Fast day with whiskey.			10	35	17.9	26.0	23.8	1.33	
20†	560	"	"	"	30	80	28.0	40.6	34.1	1.22	
21	"	"	"	"	30	80	31.5	45.7	46.8	1.49	
22	525	"	"	"	10	75	35.2	51.1	58.5	1.66	
23	560	"	"	"		80	31.5	45.7	52.4	1.66	
24	385	"	"	"		55	33.7	48.9	60.6	1.80	
25	"	"	"	"			35.4	51.4	58.0	1.64	
26	"	"	"	"			30.2	43.8	52.4	1.73	
27	"	"	"	"					50.4		
28	"	"	"	"			30.6	44.4			
29	"	"	"	"			33.3	48.3	54.0	1.62	
30	Green veg. only containing			10			31.1	45.1	53.4	1.72	
31	"	"	"	"							
Apr.											
1	"	"	"	"	20		34.2	49.6	55.2	1.62	
2	"	"	"	"	"		35.9	52.0	55.2	1.54	
3	"	"	"	"	30		35.9	52.0	64.8	1.80	
4	"	"	"	"	50						
5	"	"	"	"	70						
6	"	"	"	"	80		38.5	55.8	65.6	1.70	
7	"	"	"	"	90		41.4	60.0	52.9	1.28	
8	"	"	"	"	100		35.4	51.4	51.4	1.45	
9	"	"	"	"	150		39.4	57.2	59.5	1.51	
10	"	"	"	"	"						
11	"	"	"	"	"						
12	"	"	"	"	175						
13	"	"	"	"	"		41.7	60.5	62.1	1.49	6.60
14	"	"	"	"	"						
15	"	"	"	"	200		41.0	59.5	66.6	1.62	6.80
16	Fast day.										
17	765	33	56	25							
18	1,240	48	100	"							
19	1,670	"	147.5	"			38.7	56.1	58.5	1.51	6.63
20	"	"	"	"							
21	"	"	"	"							
22	"	"	"	"			37.8	54.8	62.1	1.64	6.97
23	"	"	"	"							
24	1,700	50	149.5	"							

* Drowsiness; hyperpnea.

† Drowsiness.

7. Case 2414—Concluded.

Date.	Total calories.	Protein.	Fat.	Carbohydrate.	NaHCO ₃ .	Alcohol.	Alveolar CO ₂ .		CO ₂ bound by 100 cc. plasma at 20°.	Ratio plasma CO ₂ mm. alv. CO ₂ .	Plasma vol. N/50 HCl.
1915		gm.	gm.	gm.	gm.	cc.	mm.	mm. × 1.45	cc.		pH
Apr. 25	Fast day.										
26	1,835	53	156.5	40							
27	1,845	55	"	"							
28	"	"	"	"							
29	"	"	"	"							
30	1,840	52.5	"	"			39.3	57.0	65.6	1.67	6.86
May 1	"	"	"	"							
2	Fast day.										
3	1,840	52.5	156.5	40							
4	1,985	75.5	162.5	"			37.2	54.0	62.3	1.67	6.77

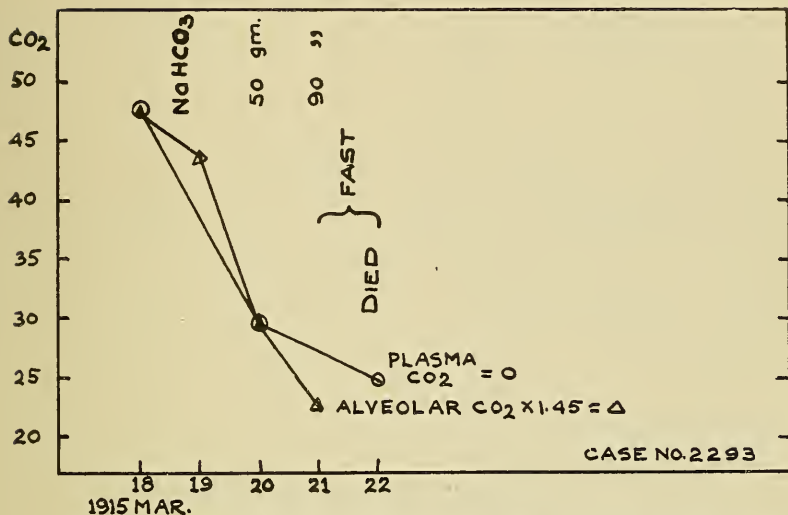


8. Case 2293.

Date.	Total calories.	Protein.	Fat.	NaHCO ₃ .	Alcohol.	Alveolar CO ₂ .		CO ₂ bound by 100 cc. plasma at 20°.	Ratio plasma CO ₂ mm. alv. CO ₂	Plasma + 1 vol. N/50 HCl.
1915		gm.	gm.	gm.	cc.	mm.	mm. $\times 1.45$	cc.		pH
Mar.										
18	1,285	41.0	71.5		65	32.4	47.0	47.3	1.46	
19	1,815	62.5	115.0		70	30.0	43.5			
20*	1,635	53.0	123.0	50	25	20.5	29.7	25.9	1.26	
21*†	Fast day.			90	35	15.8	22.9	24.9 (Death.)		
22*†	" "									

* Drowsiness; hyperpnea; nausea.

† Moribund.



8. Case 2293, male, age 29. Diabetic 2 years, of the severest type in intolerance of any food. Complicated at the end by pulmonary tuberculosis.

The curves show failure of response to large doses of NaHCO₃. Death occurred March 22, 1915.

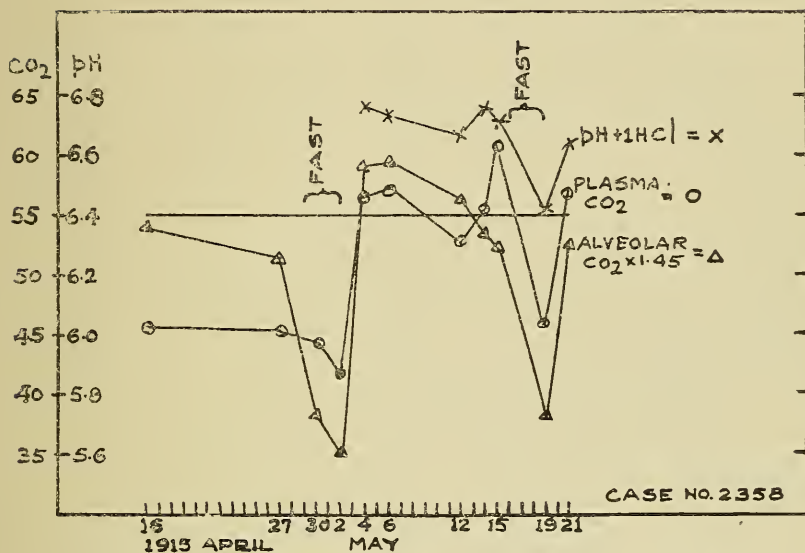
(From March 18-22, 1915.)

Group III-IV.

9. Case 2358.

Date.	Total calories.	Protein.	Fat.	Carbohydrate.	Alveolar CO ₂ .		CO ₂ bound by 100 cc. plasma at 20°.	Ratio plasma CO ₂ mm. alv. CO ₂	Plasma + vol. HCl. n/50
1915		gm.	gm.	gm.	mm.	mm. $\times 1.45$	cc.		pH
Apr. 16	1,915	62.5	178.5	0	37.2	54.0	45.8	1.23	
17	"	"	"						
18	Fast day.								
19	1,325	49.0	118.5	5					
20	"	"	"	"					
21	"	"	"	"					
22	"	"	"	"					
23	"	"	"	"					
24	"	"	"	"					
25	Fast day.								
26	1,350	50.0	119.0	10					
27	"	"	"	"	35.4	51.5	45.3	1.28	
28	325*	21.0	26.0						
29	Fast day.								
30	"	"			26.5	38.4	44.1	1.61	
May 1	"	"							
2	1,020	29.0	92.5	10	24.1	35.0	41.6	1.73	
3	1,350	50.0	119.0	"					
4	"	"	"	"	40.8	59.2	56.8	1.39	6.76
5	"	"	"	"					
6	1,375	52.0	"	15	40.7	59.0	57.0	1.40	6.73
7	1,495	52.5	131.5	"					
8	"	"	"	"					
9	Fast day.								
10	1,535	54.0	132.0	20					
11	"	"	"	"					
12	"	"	"	"	38.8	56.3	52.7	1.36	6.67
13	"	"	"	"					
14	1,595	57.0	133.0	30	36.8	53.4	55.2	1.50	6.76
15	250*	13.5	21.0		36.1	52.4	60.8	1.68	6.72
16	Fast day.								
17	"	"							
18	"	"							
19	715*	25.0	50.0	10	26.2	38.0	45.9	1.69	6.41
20	1,035	60.5	80.5	"					
21	"	"	"	"	36.0	52.2	56.9	1.58	6.64

*Partial fast.



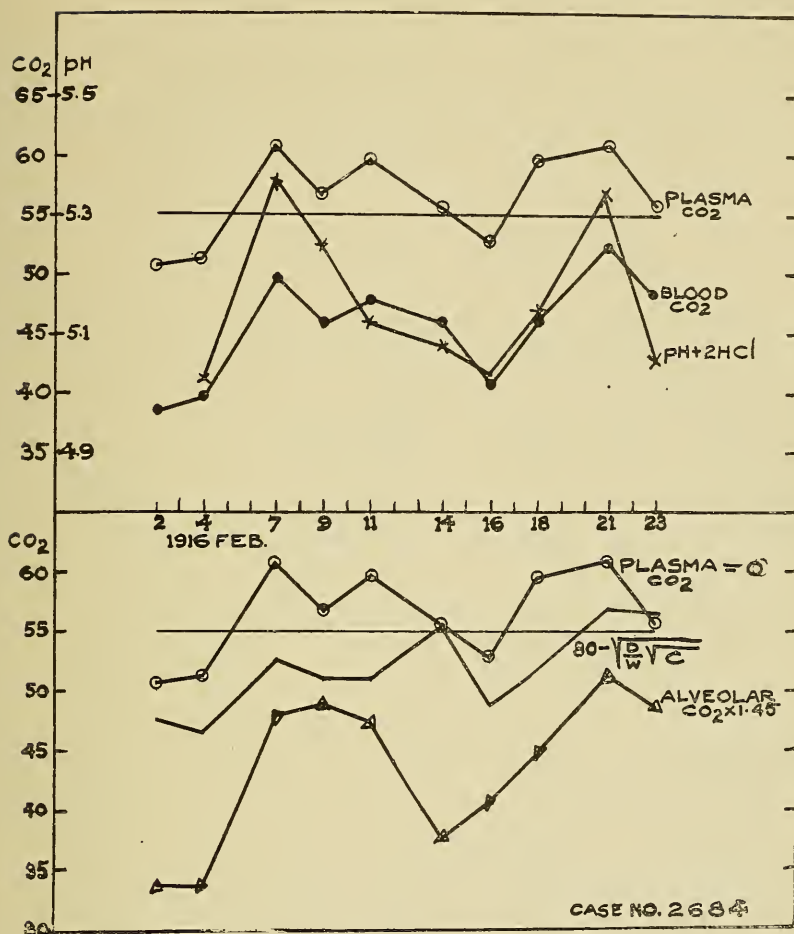
9. Case 2358, age 11. Diabetic 1 year, of severe type in intolerance of any food.

The curves show a sudden development of acidosis on two separate fasting periods of 3 days each with a return to normal on the resumption of diet.

(From April 16–May 21, 1915.)

Group III.

Date.	Diet.					Body weight. kg.	Blood.					Urine.						
	Total calories.	Protein. gm.	Fat. gm.	Carbohydrate. gm.	Alcohol. cc.		Alveolar CO ₂ .		CO ₂ bound by 100 cc. plas- ma at 20°. cc.	Ratio plasma CO ₂ mm. alv. CO ₂	CO ₂ bound by 100 cc. whole blood at 37°. cc.	Plasma + 2 vol. N/50 HCl.	Vol. per 24 hrs. cc.	Urea per liter. cc. N/10	NH ₃ per liter. cc. N/10	Acid per liter. cc. N/10	$\sqrt{\frac{W}{D}}$	$80 - \sqrt{\frac{W}{D}}$
							mm.	mm. X 1.45										
1916																		
Feb.																		
2	855	35	27.5	0	65	34.8		50.8		38.1			2,220	918	507	180	32.4	47.6
3	860	40	33.5	"	55													
4	855	45	38.5	"	45	35.3	23.1	33.5	51.1	2.21	5.01		1,790	1,425	662	152	33.5	46.5
5	850	50	43.0	"	35													
6	525	Fast day.				75												
7	850	40	40.0	"	45	35.5	33.0	47.9	60.6	1.84	5.36		1,665	1,580	532	116	27.2	52.8
8	"	"	"	"	"													
9	695	35	27.5	"	"	37.0	33.5	48.6	56.7	1.69	5.25		1,780	1,570	539	136	29.0	51.0
10	450*	12.5	9.5	"	"													
11	315	Fast day.				"	32.7	47.4	59.7	1.83	47.8	5.12	2,070	1,535	534	72	29.0	51.0
12	470*	14.5	10.5	"	"													
13	555	22.5	16.0	"	"													
14	575	27.5	"	"	"	37.0	26.1	37.8	55.2	2.11	5.08		2,280	964	365	90	24.5	55.5
15	605	32.5	16.5	"	"													
16	625	37.5	"	"	"	37.3	28.1	40.8	52.5	1.83	5.03		1,855	1,465	612	108	31.1	48.9
17	650	42.5	17.5	"	"													
18	"	"	"	"	"	38.0	30.9	44.8	59.3	1.92	5.13		2,345	1,225	445	70	28.3	51.7
19	"	"	"	"	"													
20	315	Fast day.				"												
21	650	42.5	17.5	"	"	37.2	35.3	51.2	60.9	1.72	5.34		1,545	1,408	470	84	23.0	57.0
22	680	35.0	24.0	"	"													
23	710	40.0	"	"	"	38.0	33.6	48.7	55.6	1.65	5.05		1,965	1,415	399	96	24.0	56.0



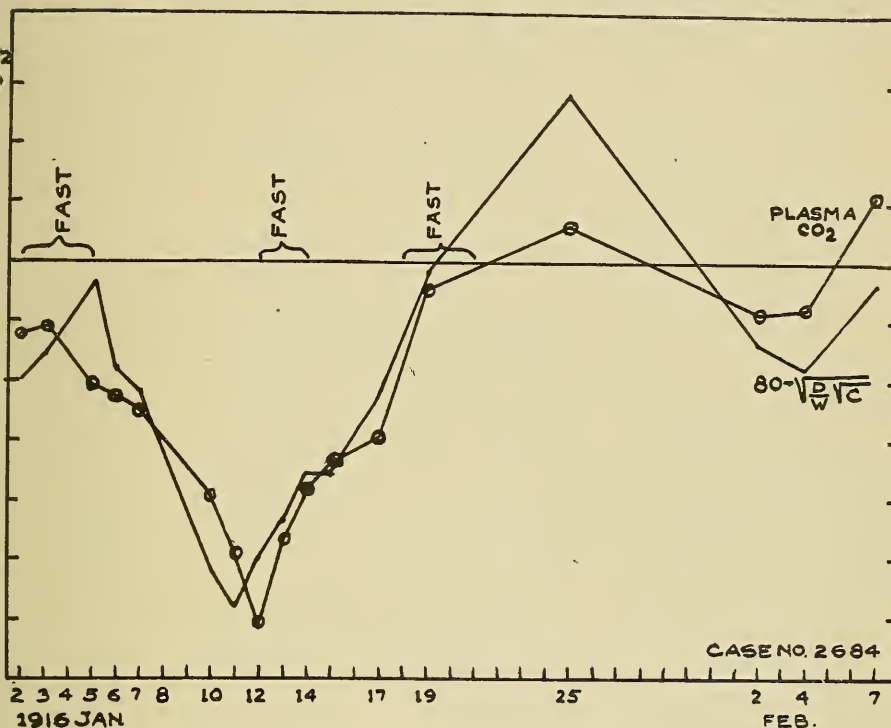
10. Case 2684, female, age 43.

The curves show a continuous low grade acidosis, possibly caused by a very low protein-fat (carbohydrate-free) diet, necessitated by a persistent glycosuria. The low level of these curves was subsequently noted over a period of 4 months' observation. The acid excretion corresponds to the plasma bicarbonate, but the alveolar CO_2 was consistently very much too low.

(From February 2-23, 1916.)

Group III.

Date.	Total calories.	Protein.	Fat.	Carbohydrate.	Alcohol.	Body weight.	CO ₂ bound by 100 cc. plas- ma at 20°.	Vol. per 24 hrs.	Urea per liter.	NH ₃ per liter.	Acid per liter.	$\sqrt{\frac{D}{W} \sqrt{C}}$	$80 - \sqrt{\frac{W}{D}}$
1916		gm.	gm.	gm.	cc.	kg.	cc.	cc.	cc. N/10	cc. N/10	cc. N/10		
Jan.													
2	Fast day.					36.0	47.8	2,150	2,120	530	230	35.0	45.0
3	"					35.3	48.2	1,615	1,475	579	250	33.0	47.0
4	"												
5	160	15	10.5	0		35.0	44.5	2,170	1,352	350	165	27.0	53.0
6	320	30	21.0	"		34.2	43.8	1,830	2,010	602	195	34.0	46.0
7	1,075	44.5	52.0	"	60	34.7	42.5	2,285	2,283	596	165	36.0	44.0
8	1,525	60.0	92.5	"	"								
9	"	"	"	"	"								
10	2,145	74.5	153.0	"	"	34.1	35.2	1,975	2,375	942	325	51.0	29.0
11	1,830	"	"	"	15	34.3	30.4	2,120	2,695	964	345	54.0	26.0
12*	Fast day.					34.7	24.6	3,355	998	678	200	50.0	30.0
13	"					33.6	31.6	2,720	785	701	185	47.0	33.0
14	160	15	10.5	0		33.3	35.9	2,300	1,010	709	148	43.0	37.0
15	240	22.5	16.0	"		33.3	38.1	2,210	1,358	734	180	43.0	37.0
16	Fast day.												
17	500*	7.5	5.5	0	60	33.2	40.0	2,520	848	574	105	36.0	44.0
18	420	Fast day.											
19	"	"			"	33.2	52.8	1,440	1,550	540	85	26.0	54.0
20	"	"			"								
21	420	Green veg. only containing		10	"								
22	525	"	"	20	75								
23	"	"	"	"	"								
24	"	"	"	25	"								
25	"	"	"	30	"	33.6	58.0	2,155	850	98	60	11.0	69.0



11. Case 2684, female, age 43 (the same case as No. 10). Diabetic of extreme severity with marked emaciation. A mild acidosis was present on admission (January 1, 1916).

The curves show a dangerous response to a moderate protein-fat (carbohydrate-free) diet, which was accompanied by clinical manifestations of severe acidosis. At the end of 9 days' fasting the patient may be considered past danger from an acidosis point of view, as is indicated by the rise of the curves. The curves show consistent parallelism between acid excretion and plasma bicarbonate.

(From January 2-25, 1916.)

Group II.

Date.	Diet.				Body weight.	Blood.		Urine.						
	Total calories.	Protein.	Fat.	Carbohydrate.		NaHCO ₃ .	CO ₂ bound by 100 cc. plasma at 20°.	CO ₂ bound by 100 cc. whole blood at 37°.	Vol. per 24 hrs.	Urea per liter.	NH ₃ per liter.	Acid per liter.	$\sqrt{\frac{D}{W} \sqrt{C}}$	$80 - \sqrt{\frac{D}{W} \sqrt{C}}$
1916 Mar. 20	625	gm. 40	gm. 47.5	gm. 7	gm.	kg.	cc.	cc.	cc.	cc. N/10	cc. N/10	cc. N/10	$\sqrt{\frac{D}{W} \sqrt{C}}$	
21*	Fast day.				30	37.0	33.3	29.9	7,740	390	312	102	42.0	38.0
22	" "					36.9	60.1	48.4	4,400	456	315	48	28.7	55.3
23	" "					37.0	45.9	38.8	3,995	442	388	68	33.4	46.6
24	120†	20	3.5			36.6	48.2	38.4	3,635	524	385	40	29.4	50.6
25	800	40	68.5			36.8	51.5	45.0	3,210	840	431	50	30.3	49.7
26	655	50	48.5											
27	600	70	33.5			37.5	50.2	42.4	3,590	1,225	412	76	31.9	48.1
28	Green veg. only containing			10		38.0	52.6	43.5	4,980	500	232	38	24.5	55.5
29	" " "		"	20		37.7	58.3	46.7	4,740	454	200	36	21.2	58.8
30	" " "		"	30										
31	" " "		"	40		36.4	63.6	52.0	5,145	400	94	24	13.3	66.7

* Drowsiness.

† Partial fast.

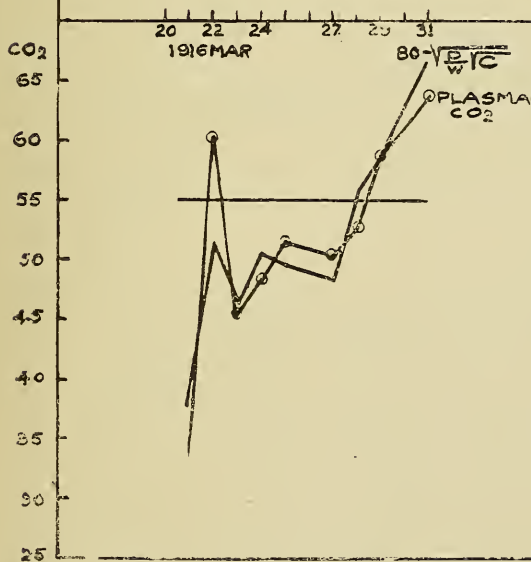
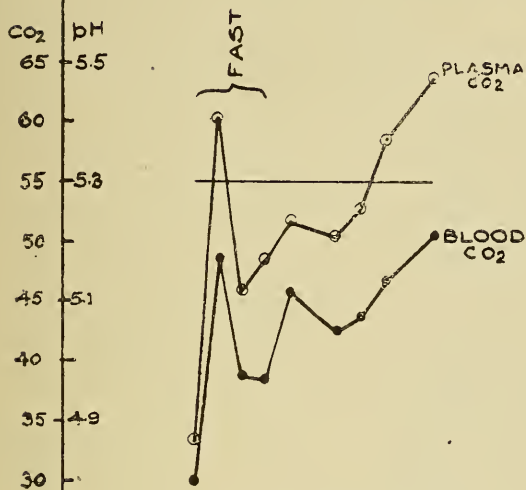
12. Case 2128, female, age 19. Diabetic 4 years, of extreme severity in the inability to metabolize carbohydrate or fat, but without marked emaciation or loss of strength. Over 2 years of observation has shown a constant low grade acidosis.

The curves show the dangerous effect of the unrestricted diet indulged in prior to her readmission, with the striking result gained by fasting and a carbohydrate tolerance test. The parallelism between acid excretion and plasma bicarbonate was also striking.

(From March 20-31, 1916.)

Group II

NaHCO₃
30 gm.



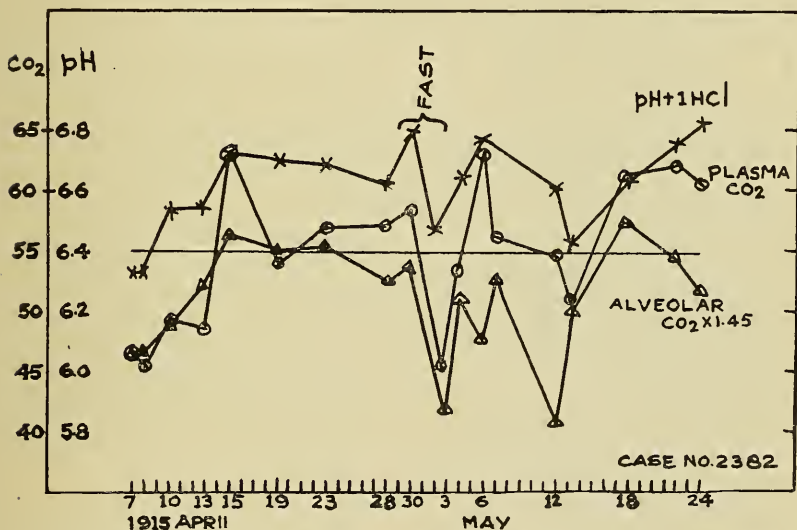
CASE NO. 2126

Date.	Total calories.	Protein.	Fat.	Carbohydrate.	Alcohol.	Alveolar CO ₂ .		CO ₂ bound by 100 cc. plas- ma at 20°.	Ratio plasma CO ₂ mm. alv. CO ₂	Plasma + 1 vol. N/50 HCl.
	gm.	gm.	gm.	cc.	mm.	mm. × 1.45	cc.			pH
1915										
Apr. 7	Green veg. only containing			15.0	15	32.0	46.4	46.3	1.45	6.33
8	"	"	"	20.0		32.2	46.7	45.3	1.41	6.32
9	"	"	"	30.0						
10	"	"	"	49.0		33.5	48.6	49.0	1.46	6.55
11*	"	"	"	19.0						
12	2,440	85.5	224.5							
13	2,440	92.5	222.0			35.9	52.1	48.4	1.35	6.55
14	2,500	97.0	226.5							
15	2,440	88.0	224.0			38.8	56.2	63.1	1.63	6.73
16	2,440	92.5	121.5							
17	2,440	85.5	224.5							
18	Fast day.									
19	2,440	92.5	221.5			38.0	55.1	54.0	1.42	6.70
20	2,440	92.5	221.5							
21	2,440	85.5	224.5							
22	2,420	93.0	219.5							
23	2,440	85.5	224.5			38.3	55.6	56.0	1.46	6.68
24	2,440	92.5	221.5							
25	Fast day.									
26	2,210	92.5	196.5							
27	2,210	92.5	196.5							
28	2,185	93.0	194.5			36.4	52.9	56.0	1.53	6.62
29	Fast day.									
30	"	"				37.0	53.7	57.3	1.55	6.80
May 1	"	"								
2	"	"								
3	Green veg. only containing			20.0		28.7	41.6	45.1	1.57	6.46
4	"	"	"	40.0		35.2	51.0	53.2	1.52	6.64
5	"	"	"	50.0						
6	"	"	"	60.0		32.7	47.4	63.0	1.93	6.75
7	"	"	"	70.0		36.4	52.8	56.0	1.54	
8	"	"	"	80.0						
9	"	"	"	90.0						
10	"	"	"	100.0						
11*	"	"	"	24.5						

13. Case 2382—Concluded.

Date.	Total calories.	Protein.	Fat.	Carbohydrate.	Alcohol.	Alveolar CO ₂ .		CO ₂ bound by 100 cc. plasma at 20°.	Ratio plasma CO ₂ mm. alv. CO ₂	Plasma vol. HCl.
1915		gm.	gm.	gm.	cc.	mm.	mm. × 1.45	cc.		pH
May 12	555	24.0	44.5	10.0		27.8	40.3	54.5	1.96	6.61
13	930	43.0	72.0	20.0		34.4	49.9	50.9	1.48	6.42
14	1,230	47.0	105.5	15.0						
15	1,370	62.0	113.5	15.0						
16	555*	21.5	49.0	3.0						
17	935*	46.5	80.0	12.5						
18	1,530	78.0	123.0	15.0		39.3	57.3	61.3	1.56	6.64
19	1,520	60.5	130.5	15.0						
20	1,450	70.0	123.5	3.5						
21	1,430	71.0	122.5							
22	1,425	60.5	127.0			37.7	54.7	62.3	1.65	6.76
23	Fast day.									
24	1,425	53.0	130.0			35.6	51.6	60.6	1.70	6.83

*Partial fast.



13. Case 2382, male, age 40. Diabetic 8 years, severe in intolerance of food, with a tendency to a low grade chronic acidosis.

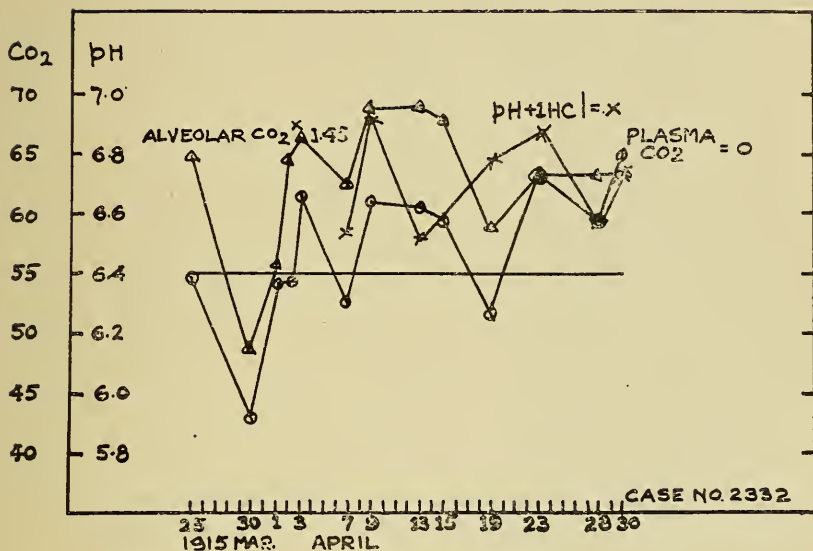
The curves are peculiar in that they are high during a period of relatively high fat feeding, and show an unstable and low level during a carbohydrate tolerance test, due perhaps to the 4 days' fast which preceded this test.

(From April 7–May 24, 1915.)

Group III.

14. Case 2332.

Date.	Total calories.	Protein.	Fat.	Carbohydrate.	Alcohol.	Alveolar CO ₂ .		CO ₂ bound by 100 cc. plasma at 20°.	Ratio plasma CO ₂ mm. alv. CO ₂	Plasma + 1 vol. N/50. HCl.
1915		gm.	gm.	gm.	cc.	mm.	mm. × 1.45	cc.		pH
Mar.										
25	1,720	91.5	58	30	97.5	44.7	64.8	54.6	1.22	
26	1,725	85.5	61	"	"					
27	"	91.5	58.5	"						
28	682	Fast day.			"					
29	2,180	111.0	99.0	30	"					
30	2,215	111.5	102.5	"	"	33.3	48.3	42.7	1.28	
31	2,250	112.5	105.5	"	"					
Apr.										
1	2,215	112.0	102.5	"	"	38.5	55.8	54.4	1.41	
2	2,385	114.0	115.0	40	"	44.6	64.7	54.4	1.22	
3	"	"	"	"	"	45.9	66.6	61.5	1.34	
4	700	Fast day.			100.0					
5	2,370	116.0	111.0	40	"					
6	2,410	114.0	116.0	"	"					
7	2,890	115.0	167.0	"	"	42.9	62.2	52.4	1.22	6.46
8	2,660	"	"	"	67.5					
9	1,920	88.0	150.0	"		47.6	69.0	61.0	1.28	6.92
10	1,975	86.0	156.5	"						
11	157	Fast day.			22.5					
12	1,975	87.0	156.5	40						
13	2,025	90.5	156.0	50		47.6	69.0	60.6	1.27	6.50
14	2,060	90.0	160.0	"						
15	2,085	91.5	173.5	"		46.8	67.7	59.5	1.27	6.59
16	2,145	90.5	169.0	"						
17	2,095	89.0	164.0	"						
18	Fast day.									
19	2,035	91.5	156.5	50		40.1	58.2	51.4	1.28	6.78
20	1,975	89.0	155.5	40						
21	2,010	79.0	174.5	"						
22	1,955	89.0	153.5	"						
23	1,945	87.5	"	"		43.5	63.1	63.1	1.45	6.84
24	1,975	90.0	155.5	"						
25	Fast day.									
26	1,970	90.0	161.0	25						
27	2,000	"	165.0	"						
28	2,165	93.5	180.5	"		43.6	63.2	59.0	1.35	6.58
29	2,110	93.0	175.0	"						
30	2,140	92.5	178.5	"		43.7	63.4	64.9	1.49	6.74



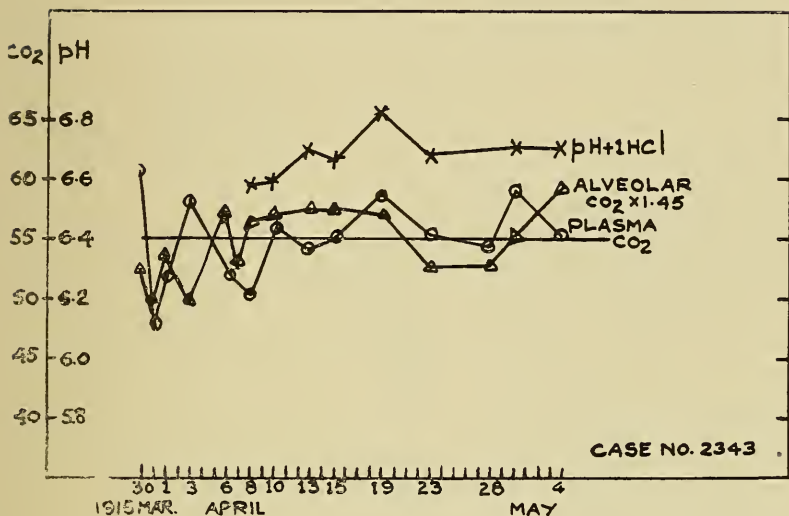
14. Case 2332, age 42. Diabetic 8 years, of mild type, complicated by furunculosis and carbunculosis.

During the period over which the chart is drawn, the patient suffered a rather intense gastrointestinal upset of unknown origin. This is reflected in the instability of the curves. Following the recovery from this attack, the curves continue on a high level up to the time of discharge from the hospital.

(From March 25-April 30, 1915.)

Group I.

Date.	Total calories.	Protein.	Fat.	Carbohydrate.	Alcohol.	Alveolar CO ₂ .		CO ₂ bound by 100 cc. plasma at 20°.	Ratio plasma CO ₂ mm. alv. CO ₂	Plasma + 1 vol. N/50 HCl.
1915		gm.	gm.	gm.	cc.	mm.	mm. $\times 1.45$	cc.		pH
Mar.										
30	1,940	98.5	83.5	15.0	100	36.2	52.2	60.5	1.67	
31	1,940	80.5	91.0	"	100	33.9	49.2	47.8	1.41	
Apr.										
1	1,965	100.0	84.0	20.0	100	37.1	53.8	51.6	1.39	
2	1,965	82.0	91.0	"	100					
3	1,970	89.5	88.0	"	100	34.4	49.9	58.2	1.69	
4	1,960	97.0	84.5	"	100					
5	2,235	108.5	109.0	19.0	100					
6	2,245	120.0	104.5	20.0	100	39.3	57.0	52.0	1.32	
7	2,240	102.0	112.0	"	100	36.4	52.8	51.4	1.41	
8	2,065	102.0	112.0	"	75	38.8	56.2	49.3	1.27	6.57
9	1,490	97.5	104.0	30.0						
10	1,510	98.5	105.5	"		39.3	57.0	56.0	1.42	6.58
11	210 Fast day.				30					
12	1,725	97.5	129.5	30.0						
13	1,955	90.0	157.5	"		39.8	57.7	54.0	1.36	6.69
14	1,970	92.0	158.5	"						
15	2,205	92.0	183.5	"		39.5	57.3	55.0	1.39	6.66
16	2,090	97.0	179.5	"						
17	2,085	89.5	182.5	"						
18	Fast day.									
19	2,215	90.0	180.5	40.0		39.3	57.0	58.5	1.49	6.82
20	2,745	104.0	231.5	"						
21	2,730	95.0	234.0	"						
22	2,715	102.5	229.0	"						
23	2,710	101.5	229.0	"		36.9	52.5	55.2	1.50	6.68
24	2,715	102.5	230.0	"						
25	Fast day.									
26	2,665	97.0	231.0	30.0						
27	2,655	97.0	230.0	"						
28	2,775	90.0	245.5	"		36.4	52.8	54.4	1.49	
29	2,755	96.5	240.5	"						
30	2,760	92.0	243.0	"		38.0	55.1	59.0	1.55	6.70
31	2,735	94.0	239.0	"						
May										
1	Fast day.									
2	2,760	93.5	242.0	30.0						
3	2,780	97.0	243.0	"						
4	2,930	101.0	257.5	"		40.8	59.2	55.4	1.36	6.70
5	3,090	104.0	273.5	"						
6	3,090	104.0	273.5	"						
7	2,580	100.5	220.0	"						



15. Case 2343, male, age 44. Diabetic 9 years, mild in type, without evidence of acidosis before the institution of active treatment.

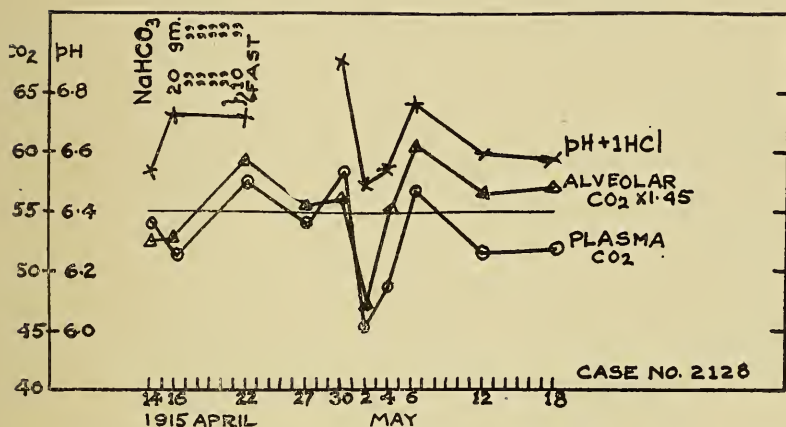
The curves show an unstable and rather low level, following a 2 months' period of very low diet, and a gradual rising and uniformity of the curves when the patient was placed on an adequate diet.

(From March 30-May 4, 1915.)

Group I.

Date.	Total calories.	Protein.	Fat.	Carbohydrate.	NaHCO ₃ .	Alveolar CO ₂ .		CO ₂ bound by 100 cc. plasma at 20°.	Ratio plasma CO ₂ mm. alv. CO ₂	Plasma + 1 vol. N/50 HCl.
1915		gm.	gm.	gm.	gm.	mm.	mm. × 1.45	cc.		pH
Apr. 15	2,040	142	145	26.5	20	35.9	52.1	54.0	1.50	6.53
16	2,830	202.5	204	26.0	"	36.4	52.8	51.4	1.41	6.72
17	2,780	155.0	223	18.0	"					
18	1,845	129.0	133	19.0	"					
19	1,370	47.0	104.5	50.5	"					
20	Fast day.				"					
21	" "				10					
22	2,005	8.0	201.5	24.0		40.8	59.2	57.5	1.41	6.72
23	2,225	32.5	186.0	89.5						
24	2,430	40.5	202.0	95.0						
25	1,000	39.0	58.0	74.0						
26	Green veg. only containing			75.0						
27	"					38.3	55.5	54.0	1.41	
28	1,855	2.6	155.5	75.0						
29	"	"	"	"						
30	930	0	100.0	0		38.7	56.1	58.8	1.52	6.92
May 1	1,440	29.5	141.5	1.0						
2	1,450	30.5	142.0	"		31.3	45.4	45.1	1.44	6.49
3	1,075	"	102.0	"						
4	1,040	26.0	100.0	"		38.0	55.1	48.6	1.28	6.55
5	815	24.0	80.0	"						
6	1,095	37.0	78.0	54.0		42.0	60.9	57.0	1.36	6.78
7	Fast day.									
8	1,095	32.5	67.0	83.0						
9	1,075	33.0	66.5	67.5						
10	1,060	29.0	66.0	81.0						
11*	175 Fast day.									
12	870	26.5	44.0	86.5		38.8	56.3	51.8	1.35	6.60
13	930	32.5	40.0	104.0						
14	875	29.5	40.0	93.0						
15	1,180	45.0	45.5	140.0						
16	465	0	50.0	0						
17	1,130	43.5	46.5	124.5						
18	950	42.0	29.0	123.5		39.3	57.0	51.9	1.32	6.57

*Alcohol, 25 cc.

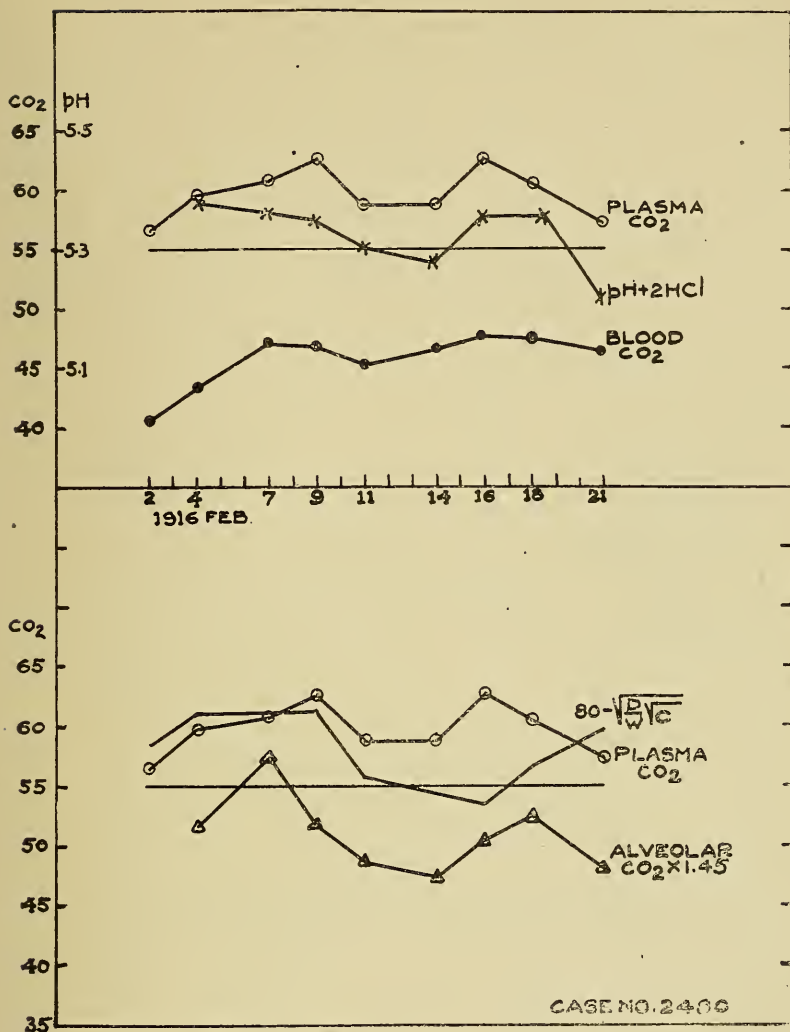


16. Case 2128, female, age 18. Diabetic 3 years, of severe type in inability to metabolize carbohydrate or fat, though maintaining a fair state of nutrition and strength.

(From April 15-May 18, 1915.)

Group III-IV.

Date.	Diet.				Body weight.	Blood.						Urine.				
	Total calories.	Protein	Fat.	Carbohydrate.		Alveolar CO ₂ .	CO ₂ bound by 100 cc. plasma at 20°.	Ratio plasma CO ₂ mm. alv. CO ₂	CO ₂ bound by 100 cc. whole blood at 37°.	Plasma + 2 vol. HCl N/50	Vol. per 24 hrs.	Urea per liter.	NH ₃ per liter.	Acid per liter.	$\sqrt{\frac{D}{W} \sqrt{C}}$	$80 - \sqrt{\frac{D}{W} \sqrt{C}}$
1916		gm.	gm.	gm.	kg.	mm.	mm. × 1.45	cc.	cc.	pH	cc.	cc. N/10	cc. N/10	cc. N/10		
Feb.	1,400	75	120	0	40.8			56.3	40.5		1,945	2,975	300	125	21.8	58.2
2	"	"	115	2.5												
3	"	"	"	"	40.5	35.5	51.3	59.6	43.1	5.38	2,065	3,435	251	120	19.0	61.0
4	"	"	"	"												
5	"	"	"	"												
6	Fast day.															
7	1,300	65	110	0	39.1	39.4	57.2	60.6	47.0	5.36						
8	"	"	"	"												
9	"	"	"	"	40.8	39.2	51.8	62.4	46.8	5.35	2,195	3,000	275	120	18.8	61.2
10	"	"	"	"												
11	"	"	"	"	41.0	33.5	48.6	58.8	45.0	5.31	1,250	4,620	540	180	24.2	55.8
12	"	"	"	"												
13	Fast day.															
14	1,300	65	110	0	40.8	32.7	47.4	58.8	46.6	5.28	920	4,890	540	184	20.9	59.1
15	"	"	"	"												
16	"	"	"	"	41.4	34.6	50.2	62.7	47.7	5.36	1,625	3,685	460	132	26.7	53.3
17	"	"	"	"												
18	"	"	"	"	41.8	36.0	52.2	60.3	47.4	5.36	1,095	5,010	586	196	23.5	56.5
19	"	"	"	"												
20	Fast day.									7						
21	1,100	65	90	0	41.4	33.4	48.0	57.1	46.3	5.22	1,400	3,375	433	140	20.4	59.6



17. Case 2480, female, age 28. Diabetic 5 years, formerly of a mild type, but latterly developing into an obstinately progressive form, with emaciation and inability to tolerate calories enough to maintain existence in an aglycosuric state. A low grade acidosis has been present for 15 months of observation.

During the period shown the patient was temporarily free from acidosis as the result of unusual response to treatment. The acid excretion corresponds to the plasma bicarbonate, but the alveolar CO₂ is consistently too low.

(From February 2-21, 1916.)

Group III.

18. Case 2234.

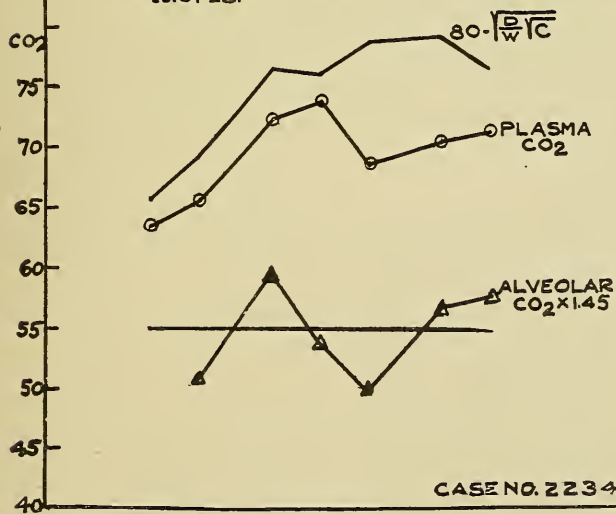
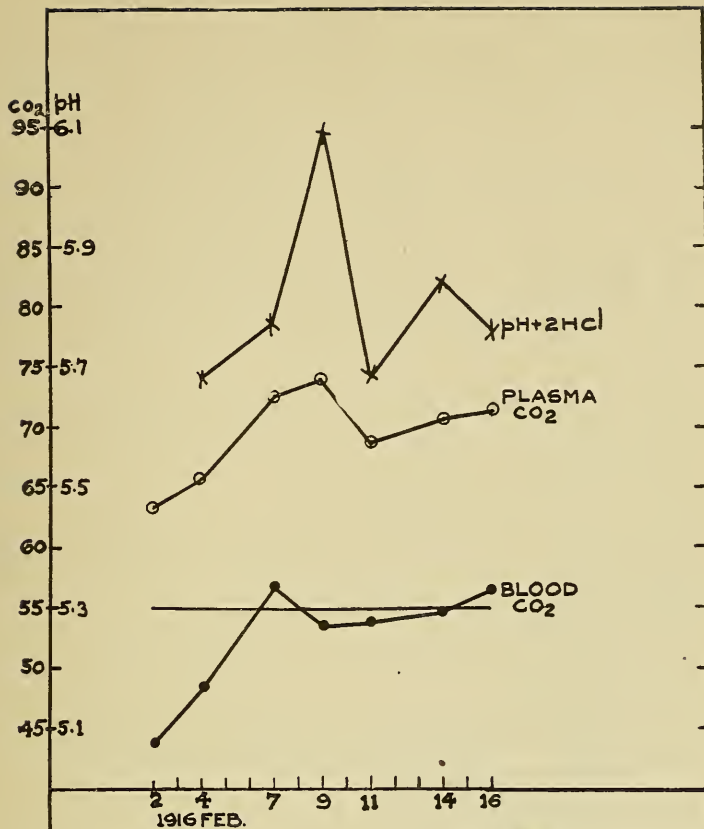
Date.	Diet.				Body weight. kg.	Blood.,						Urine.						
	Total calories.	Protein.	Fat.	Carbohydrate.		Alveolar CO ₂ .		CO ₂ bound by 100 cc. plas- ma at 20°. cc.	Ratio plasma CO ₂ mm. alv. CO ₂	CO ₂ bound by 100 cc. whole blood at 37°. cc.	pH	Plasma + 2 vol. N/50 HCl.	Vol. per 24 hrs. cc.	Urea per liter. cc. N/10 cc. N/10	NH ₃ per liter. cc. N/10 cc. N/10	Acid per liter.	$\sqrt{\frac{D}{W} \sqrt{C}}$	$80 - \sqrt{\frac{D}{W} \sqrt{C}}$
						mm.	mm. $\times 1.45$											
1916					kg.													
Feb.					48.0			63.1		43.7			740	3,380	270	300	14.2	65.8
2	Green	veg.	only	containing	48.2	34.8	50.4	65.5	1.88	48.2	5.68	1,050	3,080	128	184	10.8	69.2	
3	"	"	"	"	48.0	40.9	59.3	72.3	1.77	56.3	5.77	2,275	1,575	22	34	3.4	76.6	
4	"	"	"	"	48.2	37.0	53.6	73.9	2.0	53.2	6.09	1,975	1,460	22	34	4.0	76.0	
5	"	"	"	"	48.6	34.2	49.6	68.8	2.01	53.9	5.68	1,890	1,525	23	26	1.8	78.2	
6	"	"	"	"	48.6	39.2	56.8	70.4	2.80	54.8	5.84	2,145	1,460	18	22	1.0	79.0	
7	"	"	"	"	49.2	39.6	57.4	71.1	2.80	56.1	5.76	1,635	2,030	20	32	3.0	77.0	
8	"	"	"	"														
9	"	"	"	"														
10	"	"	"	"														
11	"	"	"	"														
12	"	"	"	"														
13	"	"	"	"														
14	"	"	"	"														
15	"	"	"	"														
16	"	"	"	"														

18. Case 2234, male, age 54. Diabetic 4 years, of the arteriosclerotic underweight type, albuminuric and cylindric, but with a normal urea index.

The chart shows the curve of typical mild diabetes without acidosis, on the diet of a carbohydrate tolerance test.

(From February 2-16, 1916.)

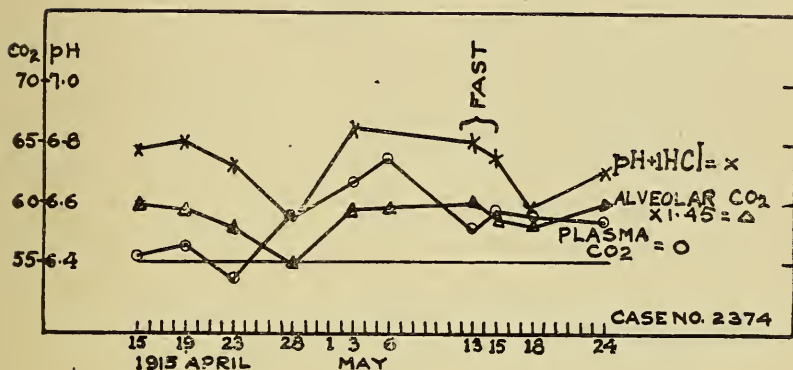
Group I



CASE NO. 2234

Date.	Total calories.	Protein.	Fat.	Carbohydrate.	Alveolar CO ₂ .		CO ₂ bound by 100 cc. plasma at 20°	Ratio plasma CO ₂ mm. alv. CO ₂	Plasma + vol. N/50 HCl.
	gm.		gm.	gm.	mm.	mm. × 1.45	cc.		pH
1915									
Apr.	Green veg. only containing			10	41.0	59.5	55.4	1.35	6.77
15	"	"	"	"					
16	"	"	"	"					
17	"	"	"	"					
18	Fast day.								
19	700	25	57.5	15	40.8	59.2	56.4	1.38	6.80
20	1,190	44.5	101.7	"					
21	"	"	"	"					
22	1,380	63.5	114.0	"					
23	"	"	"	"	39.8	57.8	33.4	1.34	6.72
24	1,325	65.0	107.5	"					
25	Fast day.								
26	1,550	65.5	131.5	15					
27	1,605	64.0	138.0	"					
28	1,530	66.0	130.0	"	37.7	54.7	59.0	1.57	6.53
29	"	"	"	"					
30	1,595	"	136.0	"					
May									
1	1,540	73.5	126.5	"					
2	Fast day.								
3	1,625	75.0	133.0	20	40.8	59.2	61.8	1.51	6.85
4	1,665	"	137.0	"					
5	1,705	67.5	145.5	"					
6	2,090	76.0	182.0	"	41.0	59.5	63.6	1.55	
7	1,975	72.5	175.0	13					
8	1,820	68.5	165.5	0					
9	Fast day.								
10	1,910	66.5	169.5	15					
11	503*	20.5	44.0	2					
12	Fast day.								
13	"	"	"	"	41.4	60.0	57.7	1.39	6.80
14	"	"	"	"					
15	675*	32.5	54.0	10	40.4	58.6	59.0	1.46	6.75
16	1,040	45.0	98.0	"					
17	1,250	63.5	102.5	"					
18	"	"	"	"	40.0	58.0	58.3	1.46	6.57
19	"	"	"	"					
20	1,260	72.5	99.5	"					
21	1,575	75.0	132.0	"					
22	1,805	83.5	153.5	"					
23	Fast day.								
24	1,570	57.0	140.0	10	40.4	60.0	58.5	1.41	6.71

*Partial fast.



19. Case 2374, age 61. Diabetic 11 years, of a mild type, apparently arrested until the year before admission, when, following a physical shock, the patient showed signs of marked acidosis.

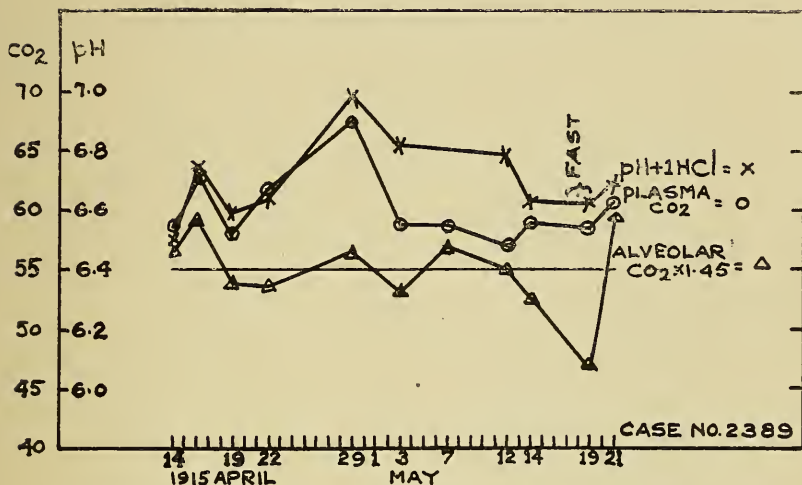
The curves illustrate the absence of acidosis in a mild diabetic responding satisfactorily to treatment.

(From April 15-May 24, 1915.)

Group I.

Date.	Total calories.	Protein.	Fat.	Carbohydrate.	Alveolar CO ₂ .		CO ₂ bound by 100 cc. plasma at 20°.	Ratio plasma CO ₂ mm. alv. CO ₂	Plasma + 1 vol. N/50 HCl.
1915		gm.	gm.	gm.	mm.	mm. × 1.45	cc.		pH
Apr.									
14	1,805	46.5	165	20	38.8	56.2	58.5	1.51	6.50
15	1,860	50.0	"	30					
16	1,815	56.5	"	20	40.7	59.0	62.6	1.54	6.75
17	1,795	"	163.5	"					
18	Fast day.								
19	1,910	46.0	176.5	20	37.2	53.9	57.5	1.55	6.58
20	"	"	"	"					
21	"	"	"	"	37.1	53.8	61.6	1.66	6.65
23	"	"	"	"					
24	"	"	"	"					
25	Fast day.								
26	1,910	46.0	176.5	20					
27	"	"	"	"					
28	2,040	60.0	185.0	"					
29	2,025	67.0	180.5	"	39.0	56.6	67.2	1.72	6.99
30	"	"	"	"					
May									
1	1,910	66.0	167.5	"					
2	Fast day.								
3	1,995	70.0	170.0	30	36.5	53.0	58.7	1.61	6.81
4	"	"	"	"					
5	1,990	61.0	173.5	"					
6	2,020	60.0	177.5	"					
7	2,025	81.0	168.5	"	39.3	57.0	58.8	1.50	
8	2,020	70.5	173.0	"					
9	Fast day.								
10	2,020	70.5	173.0	30					
11	2,045	80.0	171.0	"					
12	2,040	62.5	178.5	"	37.9	55.0	57.0	1.50	6.79
13	1,920	65.5	169.0	20					
14	1,930	69.5	172.5	"	36.1	52.4	59.0	1.63	6.62
15	"	"	"	"					
16	400*	20.0	34.0						
17	Fast day.								
18	"	"							
19	1,450*	34.0	136.0	11	32.5	46.4	58.2	1.82	6.62
20	1,805	45.0	168.0	15					
21	"	"	"	"	41.0	59.5	60.6	1.48	6.69

*Partial fast.



20. Case 2389, male, age 35. Diabetic $4\frac{1}{2}$ years, of moderate severity as shown by low tolerance for carbohydrate.

The curves show the absence of acidosis in a case which responds satisfactorily to treatment. The alveolar CO_2 following fasting on May 18-19, shows on the 19th a false drop, due not to fall in blood bicarbonate, but to the nervous effect of fasting.

(From April 14-May 21, 1915.)

Group I.

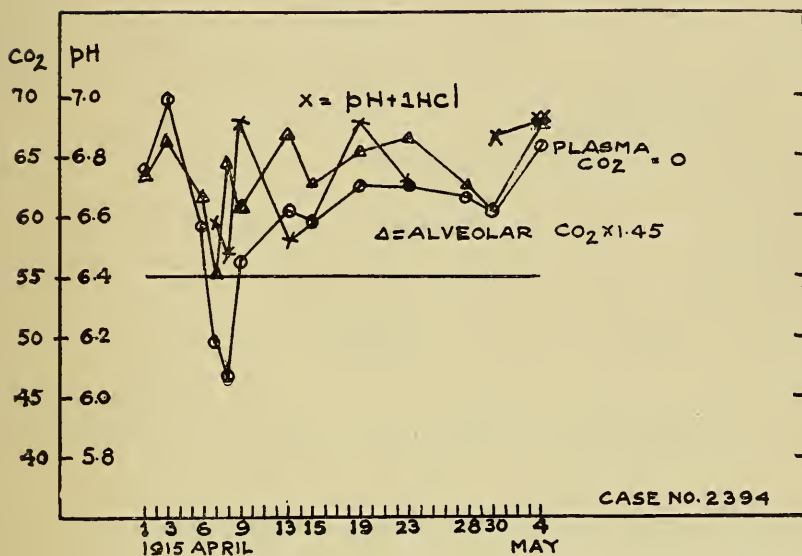
454 Blood, Urine, and Alveolar Air in Diabetes

21. Case 2394.

Date.	Total calories.	Protein.	Fat.	Carbohydrate.	Alveolar CO ₂ .		CO ₂ bound by 100 cc. plasma at 20°.	Ratio plasma CO ₂ mm. alv. CO ₂	Plasma + $\frac{1}{50}$ HCl.
1915		gm.	gm.	gm.	mm.	mm. $\times 1.45$	cc.		pH
Apr.									
1	1,175	34.5	50.0	150.0	43.6	63.2	63.2	1.45	
2	"	"	"	"					
3	1,300	40.5	45.0	175.0	45.9	66.7	69.8	1.52	
4	"	"	"	"					
5	Fast day.								
6	785	29.0	61.5	25.0	42.1	61.1	59.1	1.40	
7	1,290	50.0	106.0	"	37.7	54.7	49.4	1.31	6.59
8	1,425	70.0	111.5	"	44.6	64.7	46.3	1.04	6.47
9	1,780	69.0	150.0	"	41.7	60.5	56.4	1.35	6.92
10	"	"	"	"					
11	Fast day.								
12	2,110	76.0	171.5	50.0					
13	2,105	68.5	174.0	"	46.1	66.9	60.6	1.31	6.52
14	2,100	74.5	171.0	"					
15	2,545	71.0	220.0	"	43.2	62.6	59.5	1.38	6.60
16	2,585	76.5	221.0	"					
17	2,575	69.5	224.0	"					
18	Fast day.								
19	2,615	84.5	223.0	50	45.1	65.4	62.6	1.39	6.90
20	2,620	77.0	226.0	"					
21	2,640	80.0	228.5	"					
22	2,660	86.0	226.0	"					
23	2,710	95.5	217.5	"	45.7	66.3	62.1	1.36	6.71
24	2,715	85.0	232.5	"					
25	Fast day.								
26	2,590	84.0	219.5	50					
27	2,525	77.5	215.0	"					
28*	2,205	74.0	184.0	21	42.9	62.2	61.6	1.44	
29	Fast day.								
30	1,735**	60.5	161.0	22	41.5	60.2	60.3	1.45	6.86
May									
1	2,385	80.5	210.5	25					
2	Fast day.								
3	2,380	80.0	210.0	25					
4	2,370	79.0	209.0	"	46.6	67.6	65.9	1.41	6.91

*Alcohol, 15 cc.

**Partial fast.

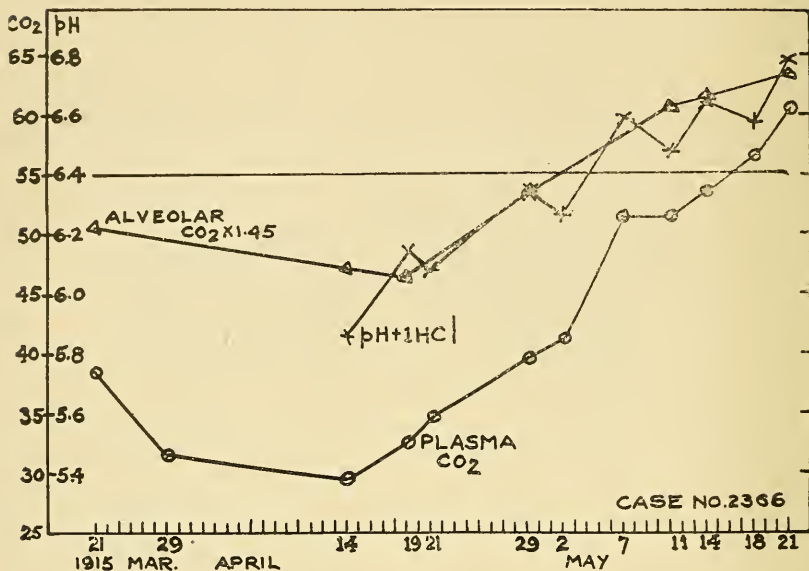


21. Case 2394, male, age 30. Diabetic $1\frac{1}{4}$ years, of mild type without any evidence of acidosis.

The chart shows a fall in the curves to below normal during the period of adjustment following a high carbohydrate diet. Following this period the curves remained normal throughout.

(From April 1-May 4, 1915.)

Group I



22. Case 2366, male, age 26. Lobar pneumonia, empyema, acute nephritis. Acute nephritis was discovered February 12, 1915, during convalescence from a severe attack of lobar pneumonia followed by empyema. Typical course of severe acute nephritis with evidence of marked change in renal function followed recovery.

The chart shows the curves in a patient with the acidosis of acute nephritis, with return to normal as renal function improved. These curves are of especial interest because they show an effect of disease on respiration exactly opposite to that often encountered in severe diabetes. The alveolar CO₂ was consistently much too high to indicate the real extent to which the alkaline reserve was lowered.

(March 21-May 21, 1915.)

Nephritic.

VITA.

GLENN ERNEST CULLEN was born April 1, 1890, at Isle St. George, Lake Erie, Ohio. He attended the public schools, passed the Boxwell Patterson examinations for a high school scholarship, and graduated from Sandusky (Ohio) High School in 1907.

He entered the University of Michigan in 1908 and was graduated in 1912 with the degree of A.B. He returned to the same University for graduate work in chemistry and engineering, and obtained the degree of B.Ch.E. in 1913.

At the University of Michigan he was assistant in Qualitative Analysis 1910-12, and teaching assistant in General Chemistry 1912-13, and was elected to Phi Lambda Upsilon and to Sigma Xi.

He has been on the Scientific Staff of The Rockefeller Institute 1913-17, and is now an Associate in the Physiological Chemistry Laboratory of The Rockefeller Institute Hospital. He is a member of the American Chemical Society and of the American Society of Biological Chemists.

He matriculated in the Faculty of Pure Science of Columbia University in 1914.

He has collaborated in the following publications:

The Mode of Action of Urease and of Enzymes in General,

D. D. Van Slyke and G. E. Cullen,

Jour. Biol. Chem., 1914, xix, 141.

A Permanent Preparation of Urease, and Its Use in the Determination of Urea,

D. D. Van Slyke and G. E. Cullen,

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The Determination of Urea by the Urease Method,

D. D. Van Slyke and G. E. Cullen,

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A. W. M. Ellis, G. E. Cullen, and D. D. Van Slyke,

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The Formation of Urea in the Liver,

D. D. Van Slyke, G. E. Cullen, and F. C. McLean,

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D. D. Van Slyke, E. Stillman, and G. E. Cullen,

Proc. Soc. Exper. Biol. and Med., 1915, xii, 165.

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